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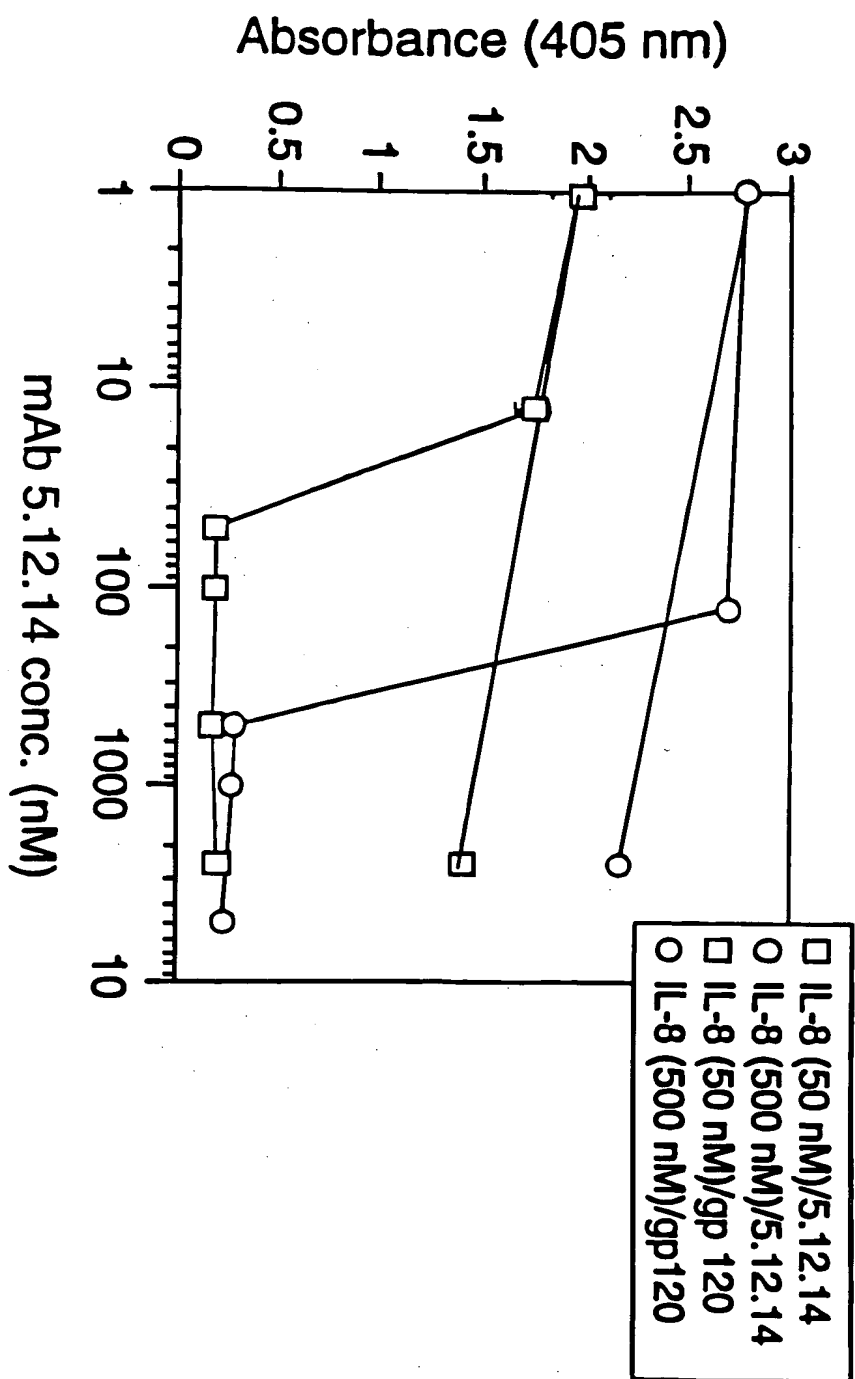
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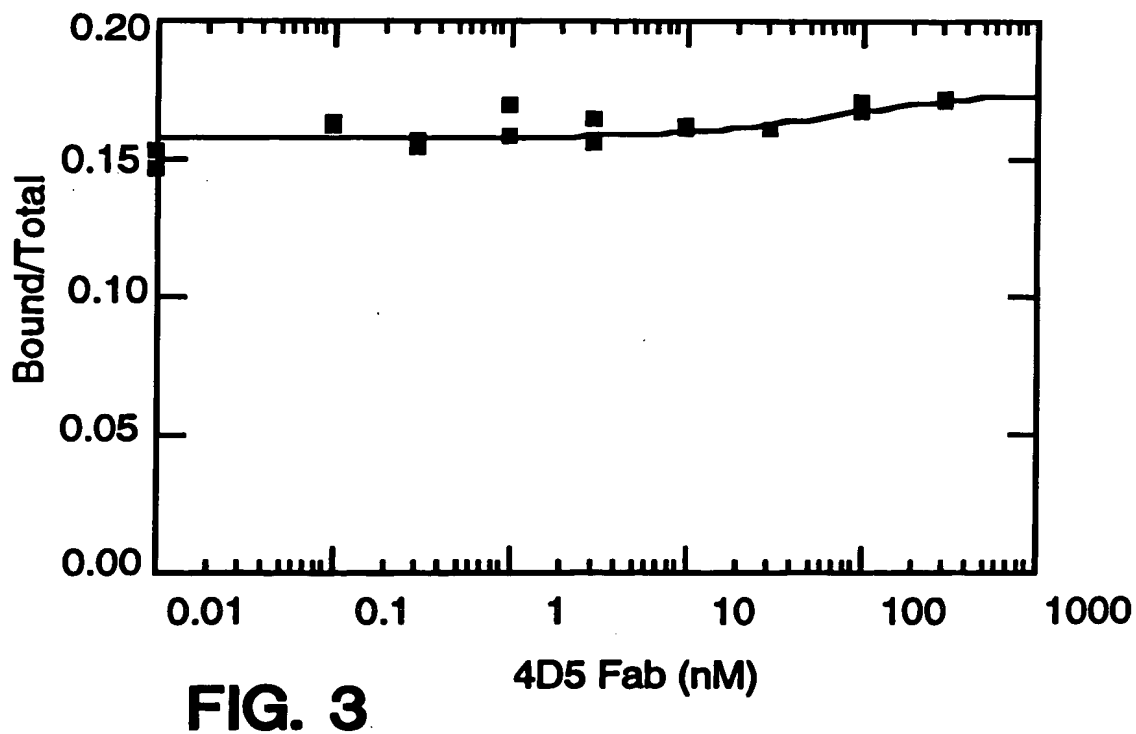
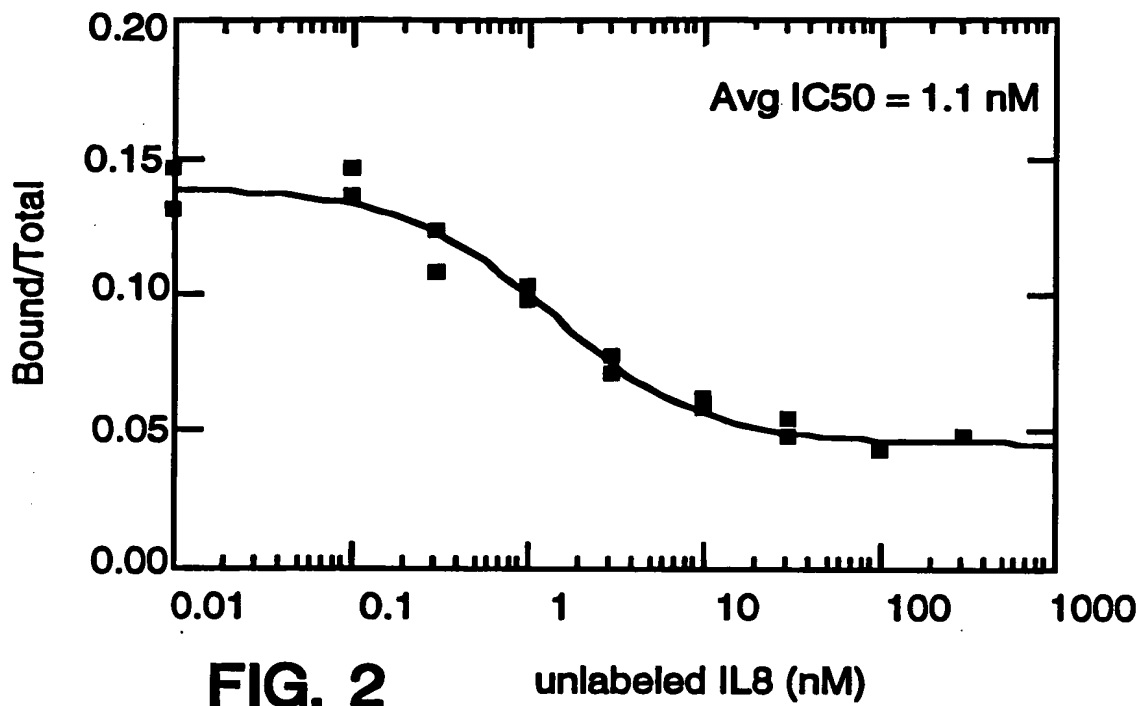
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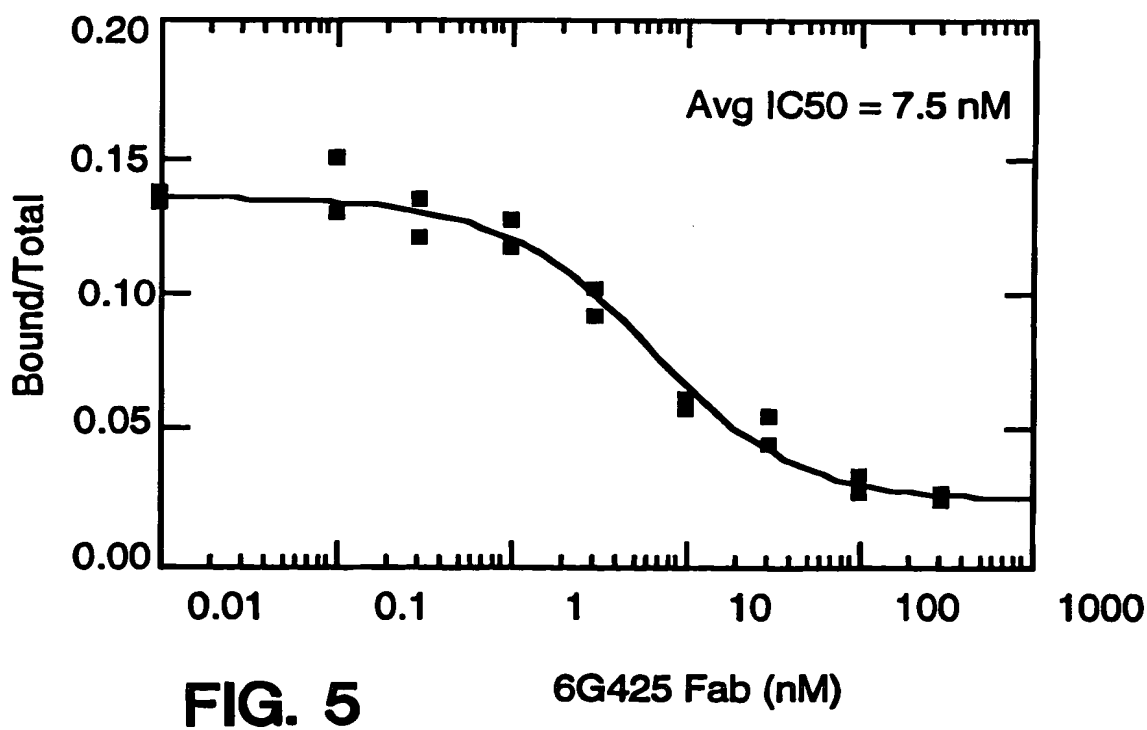
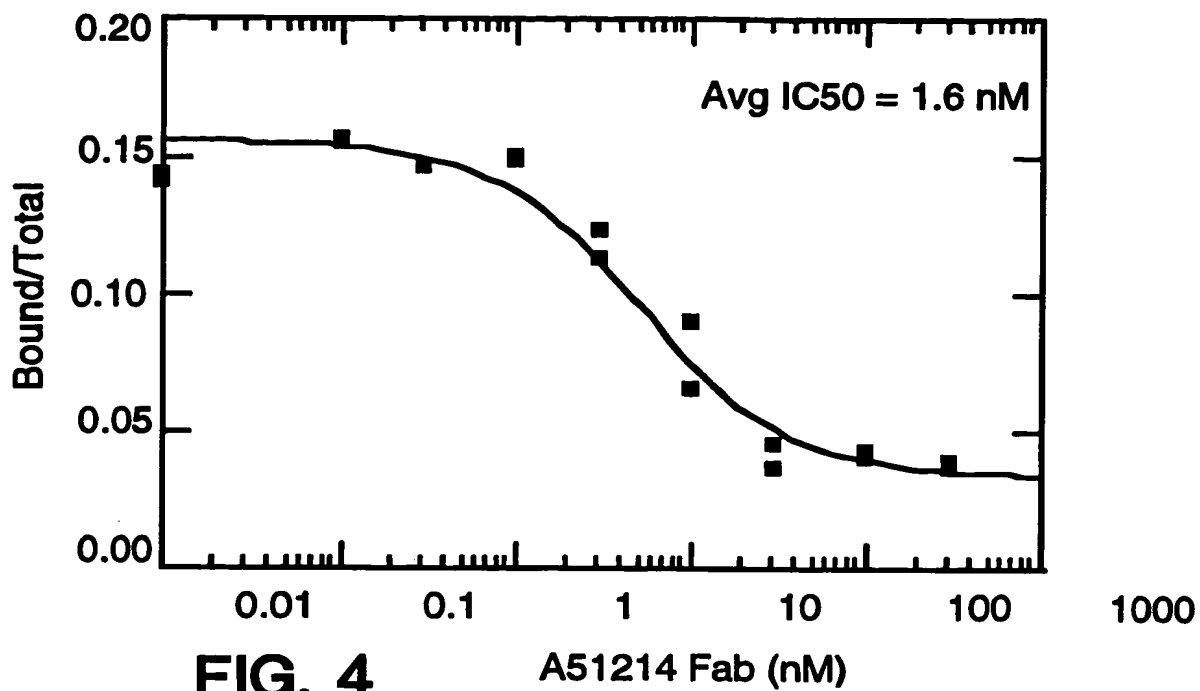
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FIG. 1







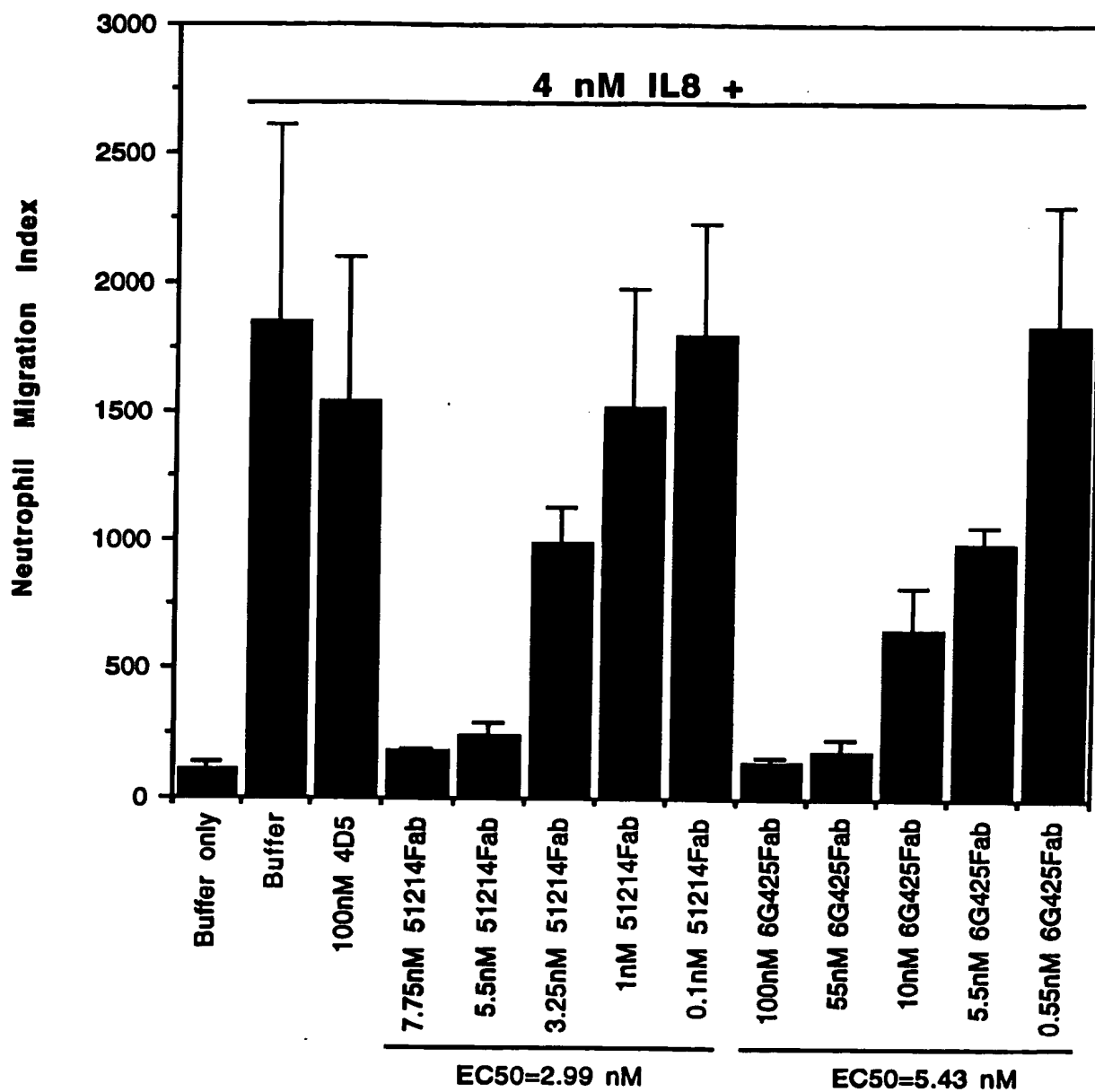


FIG. 6

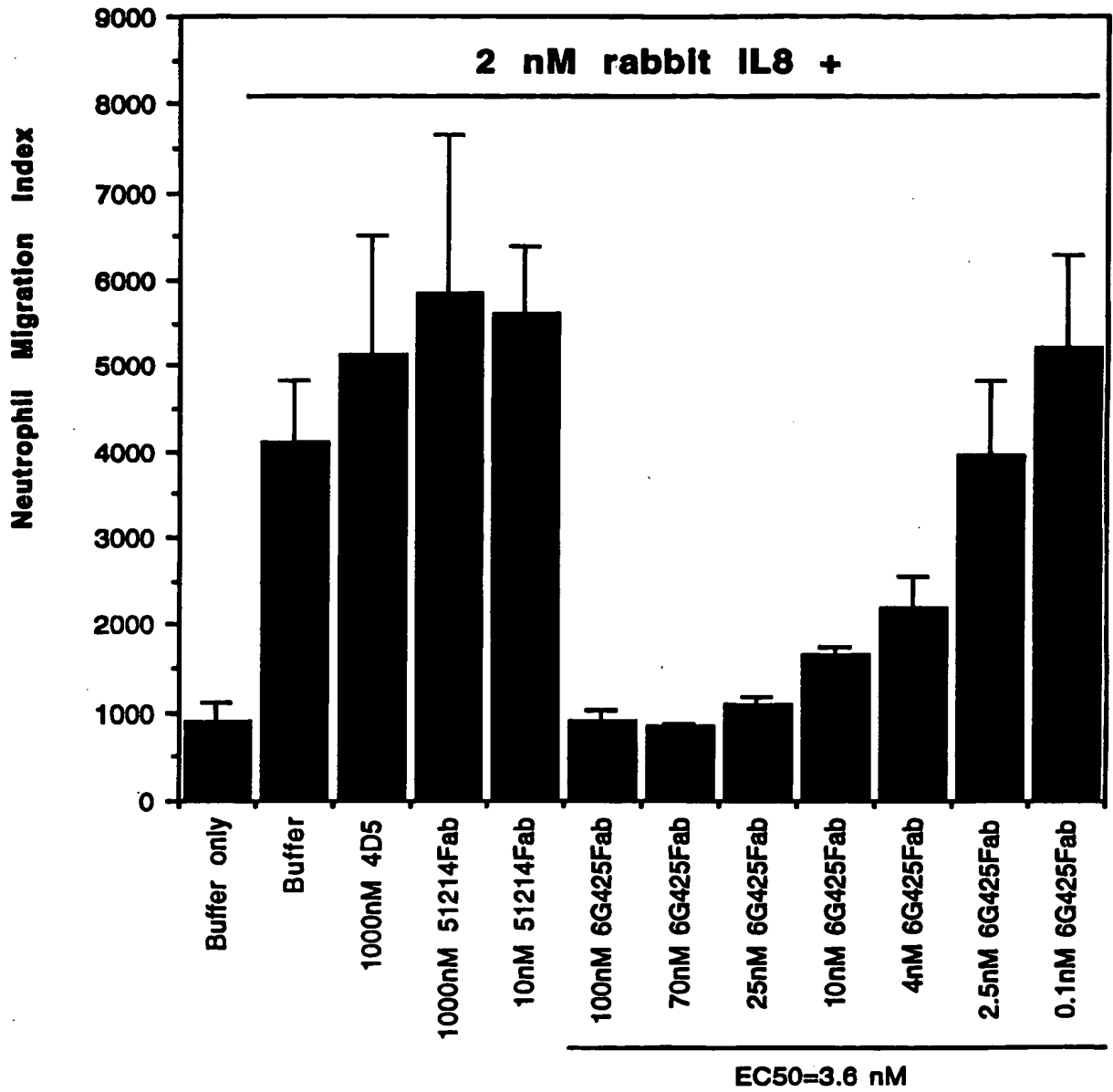


FIG. 7

Absorbance (405 nm)

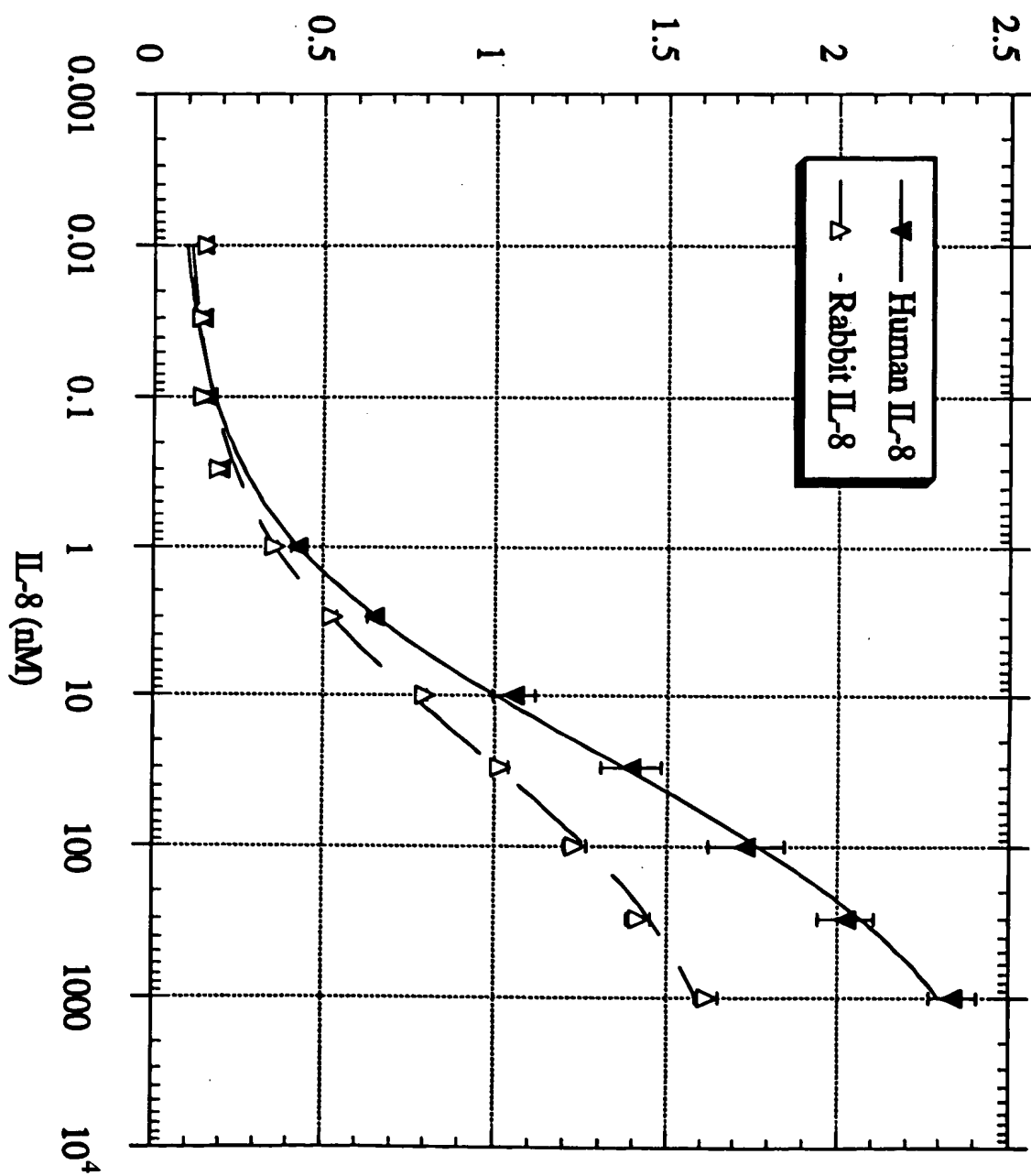


FIG. 8

% IL-8-Stimulated Elastase Release

FIG. 9

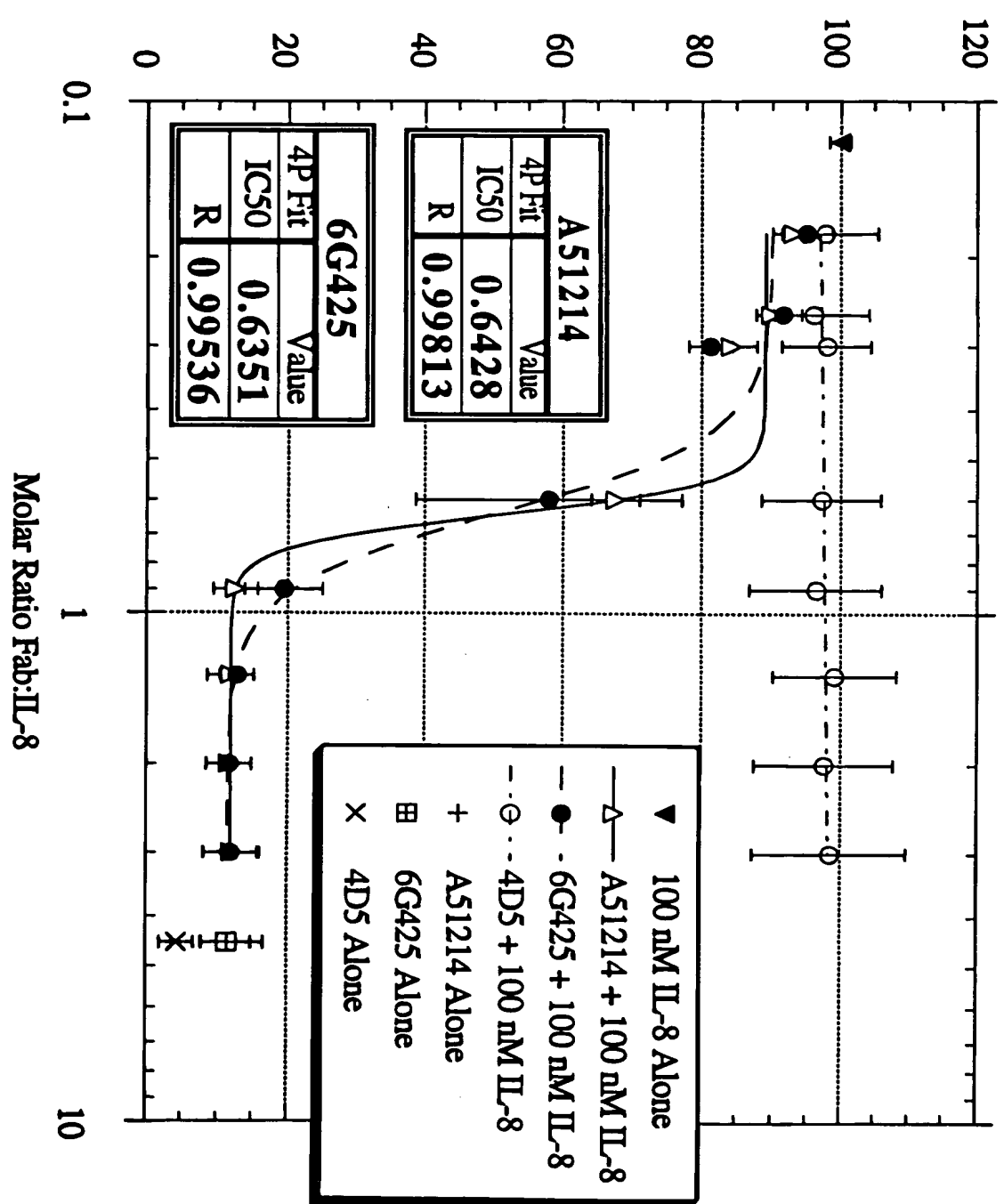
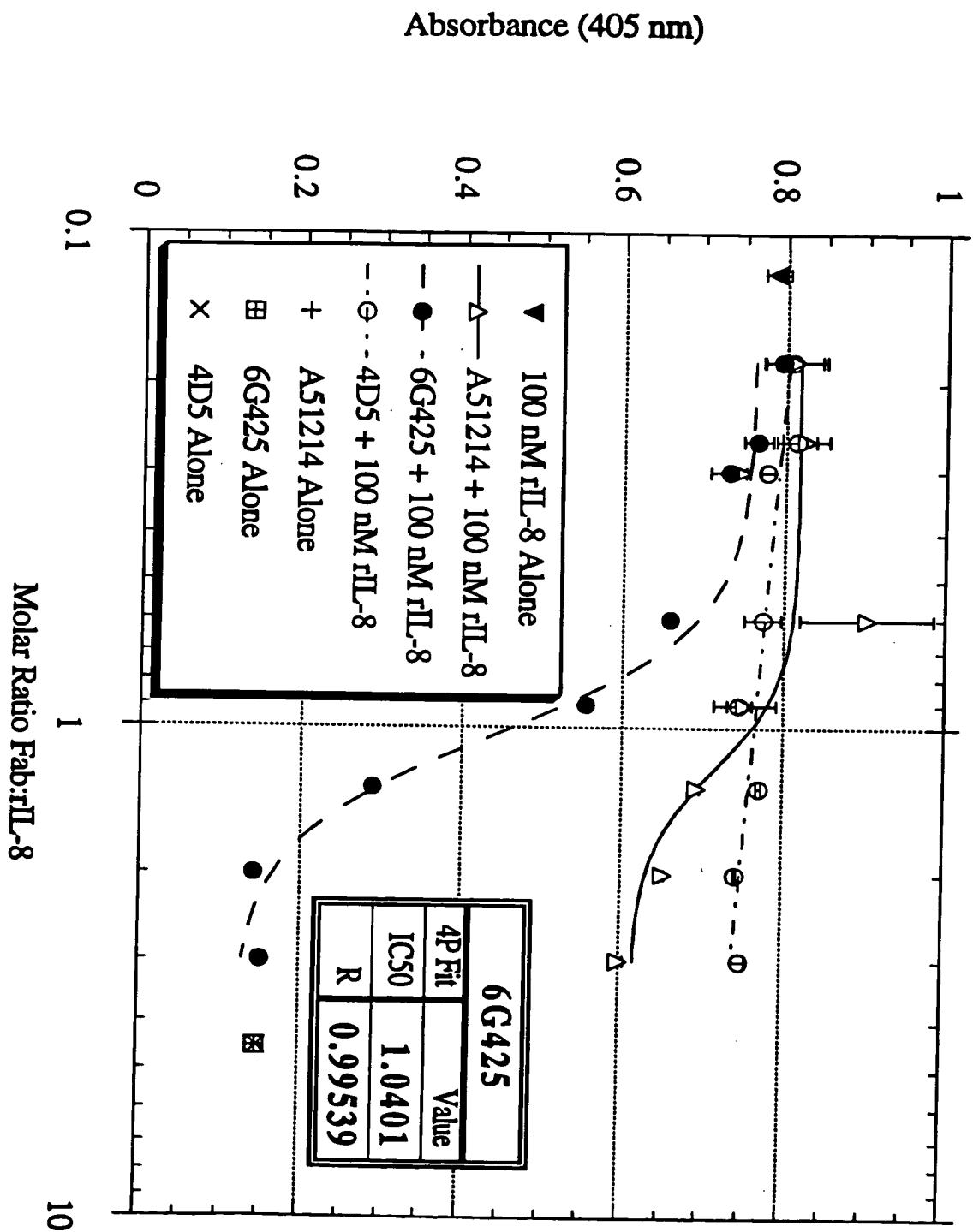


FIG. 10



MYELOPEROXIDASE

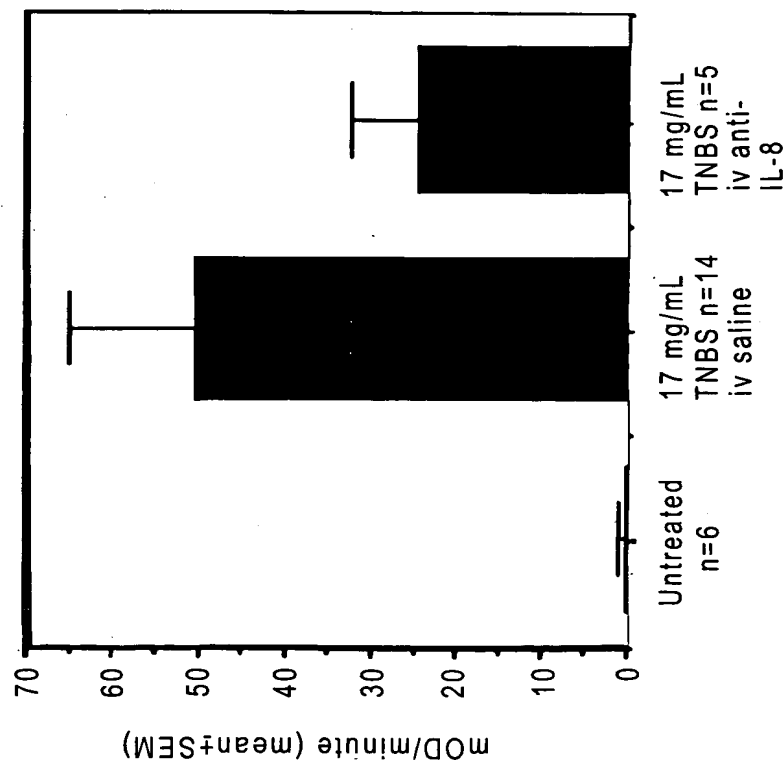


FIG. 11A

IL-8Z

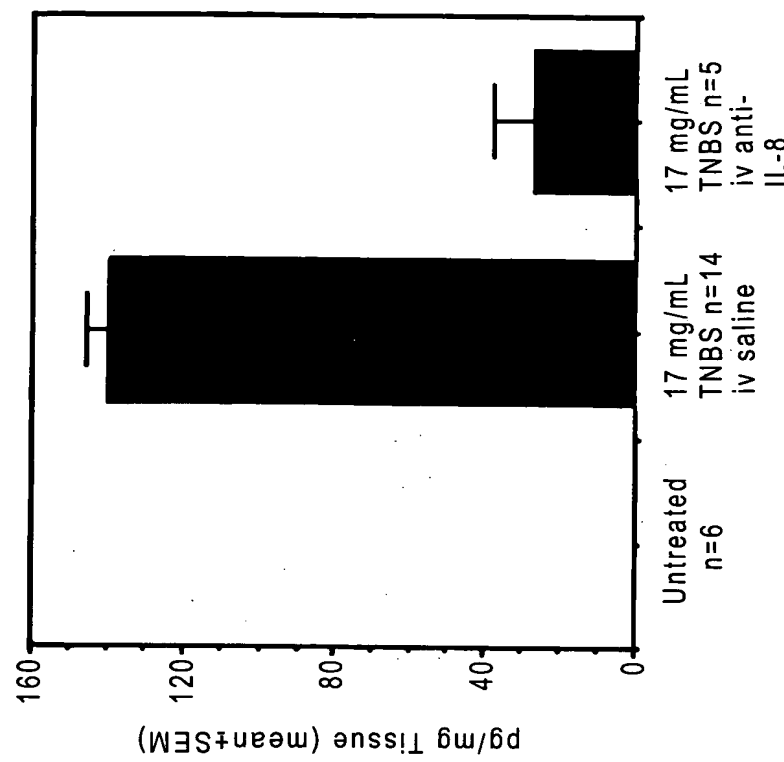


FIG. 11B

COLON WEIGHT

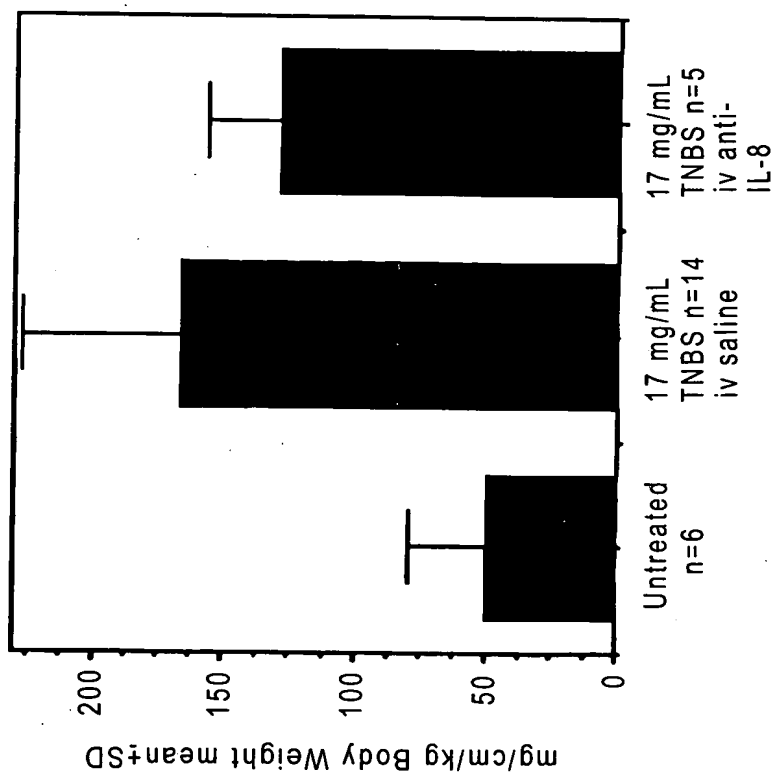


FIG. 11C

GROSS INFLAMMATION

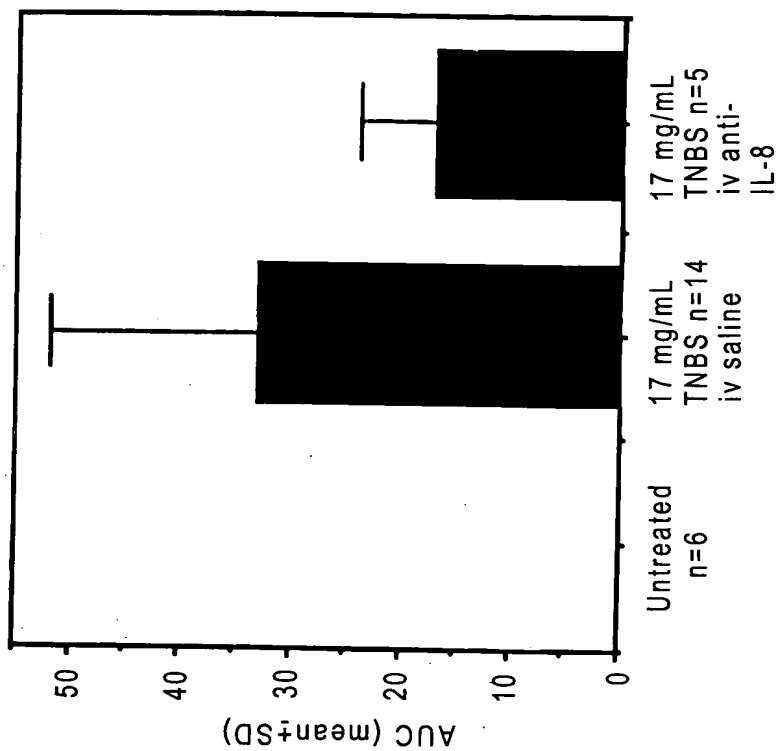


FIG. 11D

EDEMA

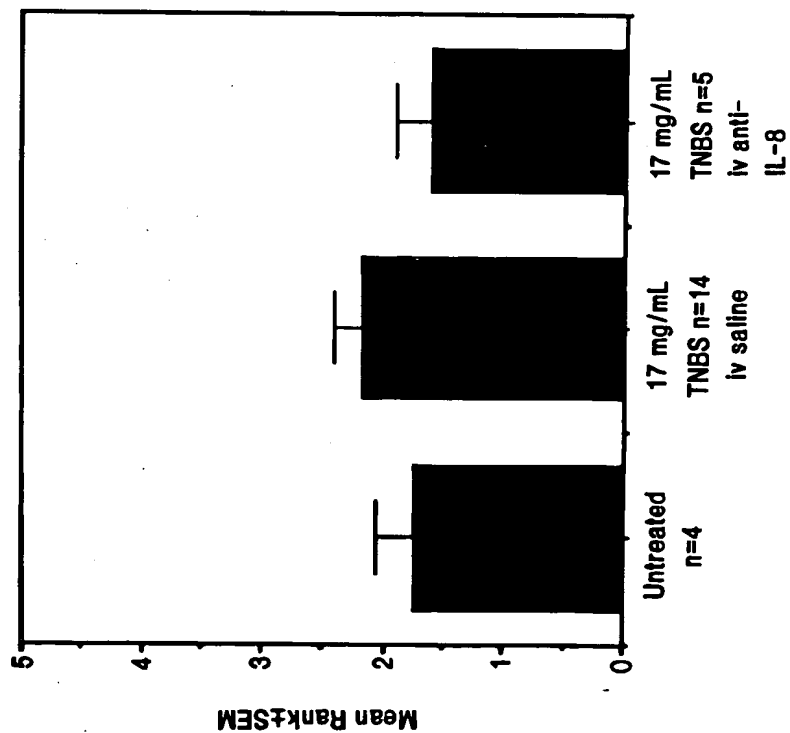


FIG. 11E

EXTENT OF NECROSIS

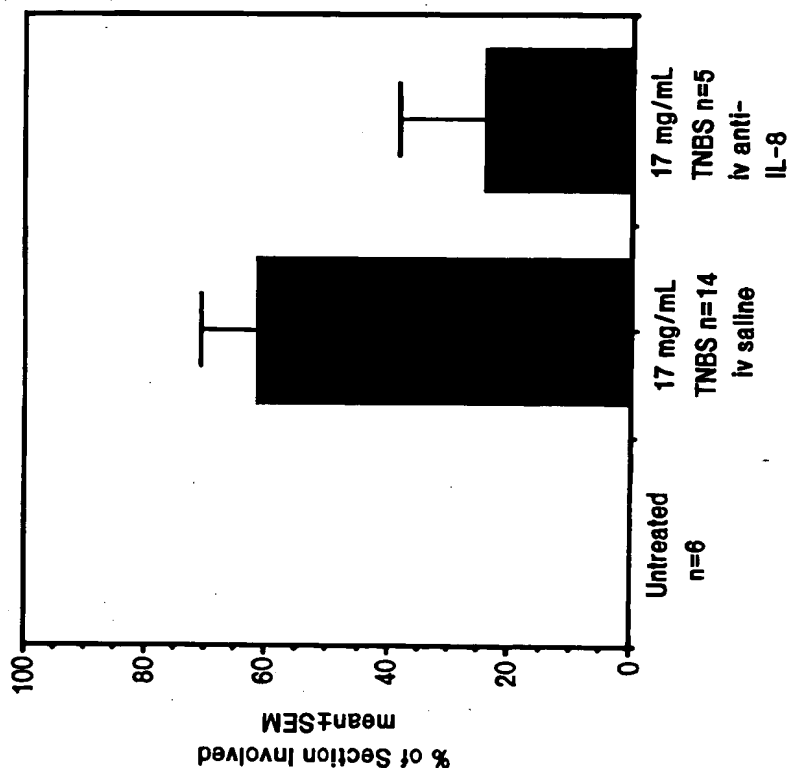


FIG. 11F



SEVERITY OF NECROSIS

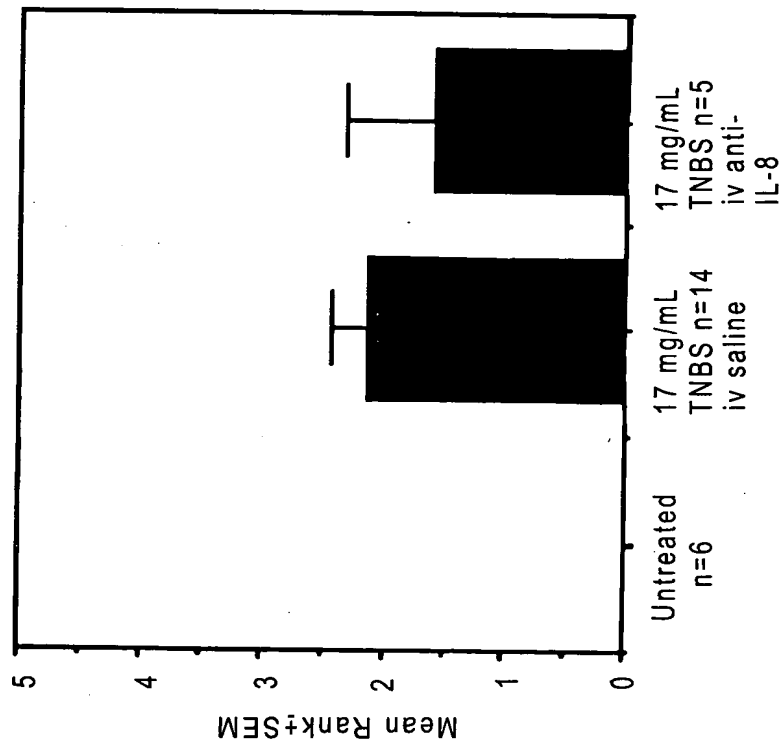


FIG. 11G

NEUTROPHIL MARGINATION

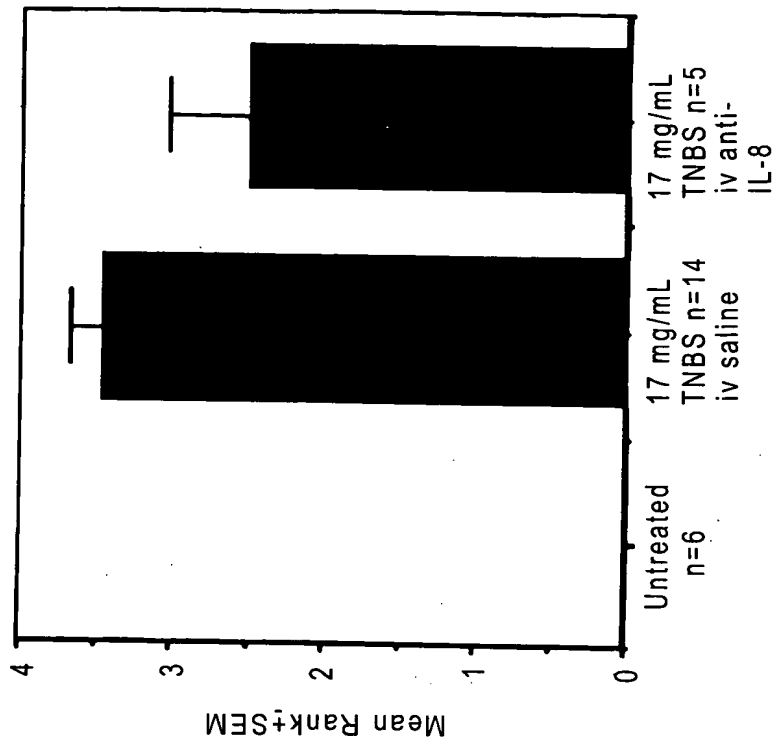


FIG. 11H

NEUTROPHIL INFILTRATION

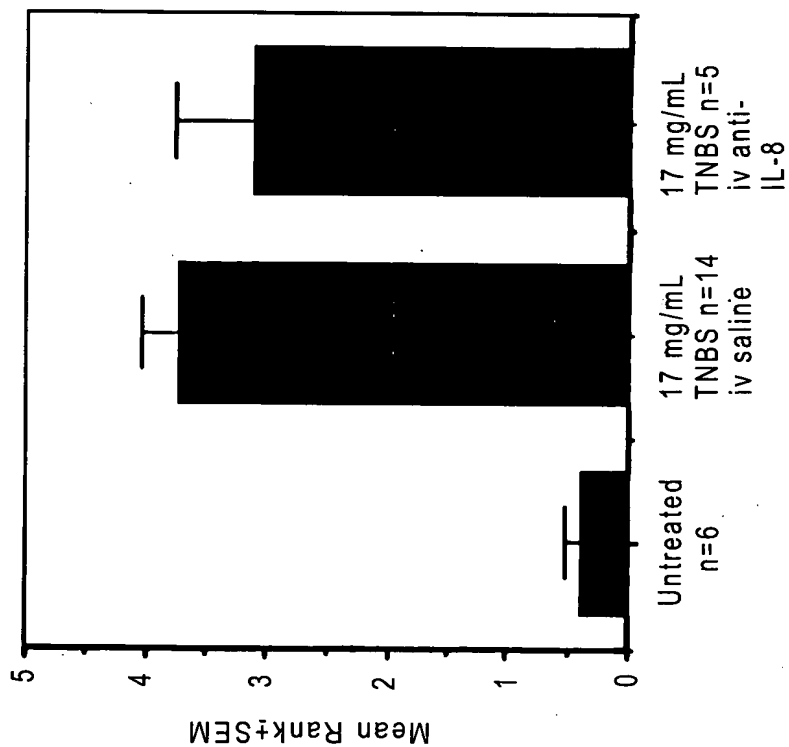


FIG. 11I

MONONUCLEAR INFILTRATION

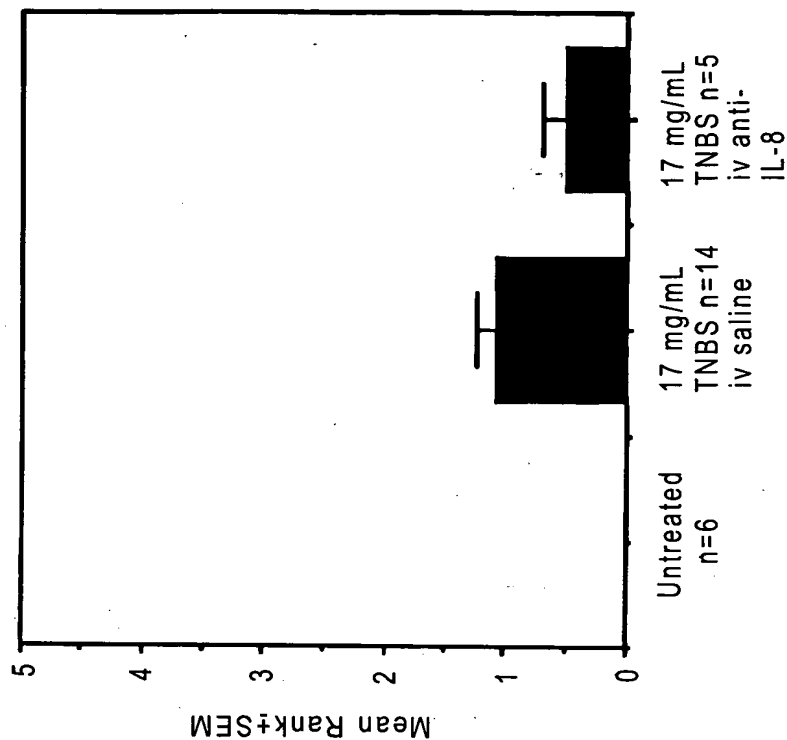
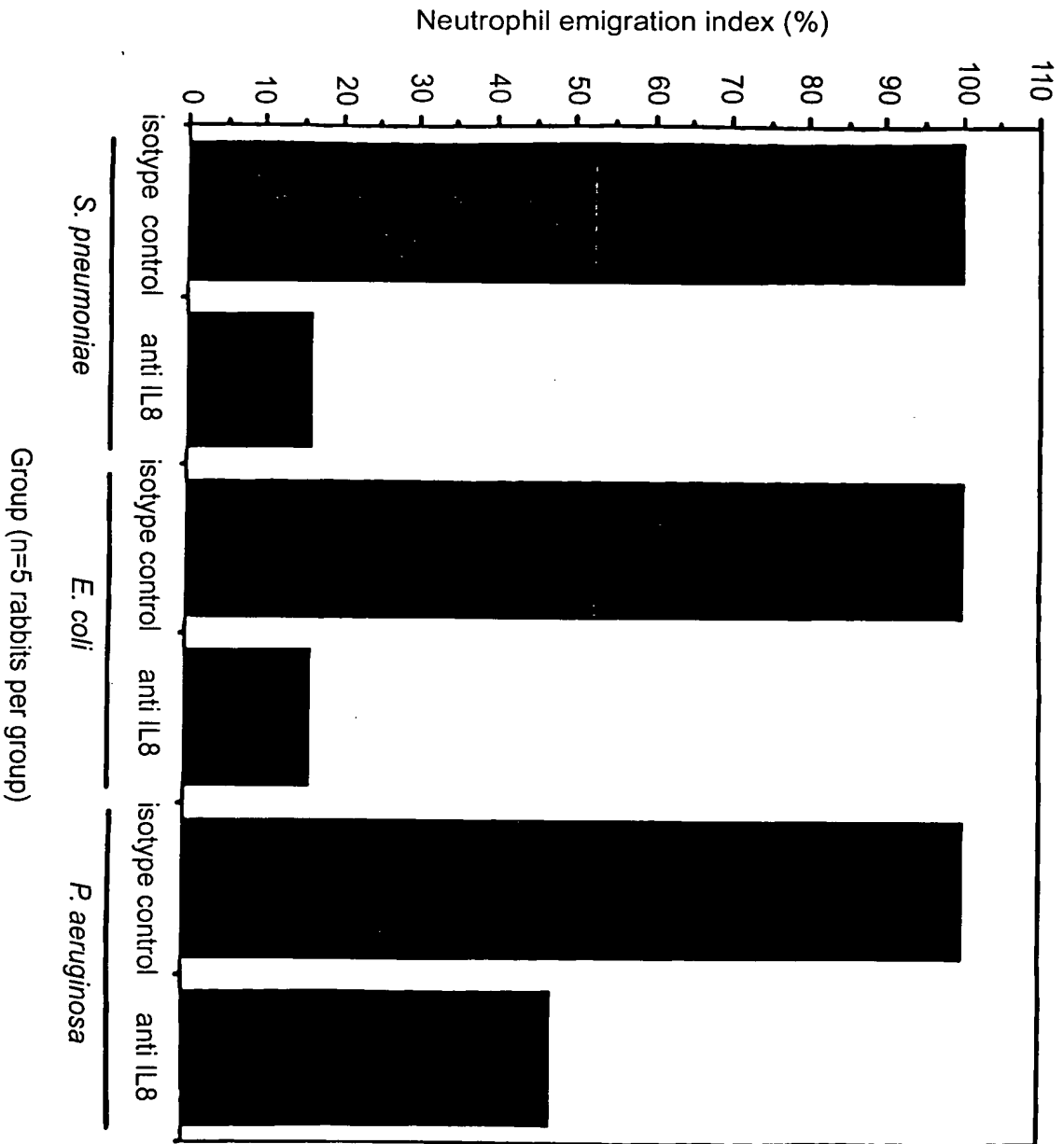


FIG. 11J



FIG. 12





Light Chain Primers:

MKLC-1, 22mer

5' CAGTCCAACCTGTTCAGGACGCC 3'

MKLC-2, 22mer

5' GTGCTGCTCATGCTGTAGGTGC 3'

MKLC-3, 23mer

5' GAAGTTGATGTCTTGTGAGTGGC 3'

Heavy Chain Primers:

IGG2AC-1, 24mer

5' GCATCCTAGAGTCACCGAGGAGCC 3'

IGG2AC-2, 22mer

5' CACTGGCTCAGGGAAATAACCC 3'

IGG2AC-3, 22mer

5' GGAGAGCTGGGAAGGTGTGCAC 3'

FIG. 13



Light chain forward primer

SL001A-2 35 mer

5' ACAAACGCGTACGCT GACATCGTCATGACCCAGTC 3'
 T T T
 A

Light chain reverse primer

SL001B 37 mer

5' GCTCTTCGAATG GTGGGAAGATGGATACAGTTGGTGC 3'

FIG. 14



Heavy chain forward primer

SL002B 39 mer

5' CGATGGGCCCCG ATAGACCGATGGGGCTGTTGTTTTGGC 3'

T C
G
A

Heavy chain reverse primer

SL002B 39-MER

5' CGATGGGCCCCG ATAGACCGATGGGGCTGTTGTTTTGGC 3'

T
A
G

FIG. 15



1 GACATTGTCA TGACACAGTC TCAAAAATTC ATGTCCACAT CAGTAGGAGA CAGGGTCAGC
CTGTAACAGT ACTGTGTCAG AGTTTTTAAG TACAGGTGTA GTCATCCTCT GTCCCAAGTCG
1 D I V M T Q S Q K F M S T S V G D R V S

61 GTCACCTGCA AGGCCAGTCA GAATGTGGT ACTAATGTAG CCTGGTATCA ACAGAAACCA
CAGTGGACGT TCCGGTCAGT CTTACACCCA TGATTACATC GGACCATAGT TGTCCTTTGGT
21 V T C K A S O N V G T N V A W Y Q Q K P
* * * * *

CDR #1

121 GGGCAATCTC CTAAGCACT GATTACTCG TCATCCTACC GGTACAGTGG AGTCCCTGAT
CCCGTTAGAG GATTTCGTGA CTAATGAGC AGTAGGATGG CCATGTCACC TCAGGGACTA
41 G Q S P K A L I Y S S Y R Y S G V P D
* * * * *

CDR #2

181 CGCTTCACAG GCAGTGGATC TGGGACAGAT TTCACTCTCA CCATCAGCCA TGTGCAGTCT
GCGAAGTGTC CGTCACCTAG ACCCTGTCTA AAGTGAGAGT GGTAGTCGGT ACACGTCAGA
61 R F T G S G S G T D F T L T I S H V Q S

241 GAAGACTTGG CAGACTATTT CTGTCAGCAA TATAACATCT ATCCTCTCAC GTTCGGTCCCT
CTTCTGAACC GTCTGATAAA GACAGTCGTT ATATTGTAGA TAGGAGAGTG CAAGCCAGGA
81 E D L A D Y F C Q Q X N I Y P L T F G P
* * * * *

CDR #3

301 GGGACCAAGC TGGAGTTGAA ACGGGCTGAT GCTGCACCAC CAACGTGTATC CATCTTCCCA
CCCTGGTTCTG ACCTCAACTT TGCCCGACTA CGACGTGGTG GTTGACATAG GTAGAAGGGT
101 G T K L E L K R A D A A P P T V S I F P

BstBI

361 CCATTCGAA

GGTAAGCTT

121 P F E

FIG. 16



1 TTCTATTGCT ACAAACGCGT ACGCTGAGGT GCAGCTGGTG GAGTCTGGGG GAGGCTTAGT
AAGATAACGA TGTTTGCGCA TCGGACTCCA CGTCGACCAC CTCAGACCCC CTCCGAATCA
1 E V Q L V E S G G G L V

61 GCCGCCTGGA GGGTCCCTGA AACTCTCCTG TGCAGCCTCT GGATTCATAT TCAGTAGTTA
CGGCGGACCT CCCAGGGACT TTGAGAGGAC ACGTCGGAGA CCTAAGTATA AGTCATCAAT
13 P P G G S L K L S C A A S G F I F S S Y
* *

CDR #1

121 TGGCATGTCT TGGGTTCGCC AGACTCCAGG CAAGAGCCTG GAGTTGGTCTG CAACCATTA
ACCGTACAGA ACCCAAGCGG TCTGAGGTCC GTTCTCGGAC CTCAACCAGC GTTGGTAATT
33 G M S W V R Q T P G K S L E L V A T I N
* * *

181 TAATAATGGT GATAGCACCT ATTATCCAGA CAGTGTGAAG GGCCGATTCA CCATCTCCCG
ATTATTACCA CTATCGTGGA TAATAGGTCT GTCACACTTC CCGGCTAAGT GGTAGAGGGC
53 N N G D S T Y Y P D S V K G R F T I S R
* * * * *

CDR #2

241 AGACAATGCC AAGAACACCC TGTACCTGCA AATGAGCAGT CTGAAGTCTG AGGACACAGC
TCTGTTACGG TTCTTGTGGG ACATGGACGT TTA CTGCA GACTTCAGAC TCCTGTGTCG
73 D N A K N T L Y L Q M S S L K S E D T A

301 CATGTTTTAC TGTGCAAGAG CCCTCATTAG TTCGGCTACT TGGTTTGGTT ACTGGGGCCA
GTACAAAATG ACACGTTCTC GGGAGTAATC AAGCCGATGA ACCAAACCAA TGACCCCGGT
93 M F Y C A R A L I S S A T W F G Y W G Q
* * * * *

CDR #3

361 AGGGACTCTG GTCAGTGTCT CTGCAGCCAA AACAAACAGCC CCATCTGTCT
TCCCTGAGAC CAGTGACAGA GACGTCGGTT TTGTTGTCGG GGTAGACAGA
113 G T L V T V S A A K T T A P S V Y

ApaI

411 ATCCGGG
TAGGCCC

130 P

FIG. 17



VL.front 31-MER

5' ACAAACGCGTACGCTGATATCGTCATGACAG 3'
VL.rear 31-MER

5' GCAGCATCAGCTCTTCGAAGCTCCAGCTTGG 3'

VH.front.SPE 21-MER

5' CCACTAGTACGCAAGTTCACG 3'

VH.rear 33-MER

5' GATGGGCCCTTGGTGGAGGCTGCAGAGACAGTG 3'

FIG. 18



1 ATGAAGAAGA ATATCGCATT TCTTCTTGCA TCTATGTTTCG TTTTCTCTAT TGCTACAAAC
TACTTCTTCT TATAGCGTAA AGAAGAACGT AGATACAAGC AAAAAAGATA ACGATGTTTG
-23 M K K N I A F L L A S M F V F S I A T N

61 GCGTACGCTG ATATCGTCAT GACACAGTCT CAAAAATTCA TGTCCACATC AGTAGGAGAC
CGCATGCGAC TATAGCAGTA CTGTGTCAGA GTTTTAAAGT ACAGGTGTAG TCATCCTCTG
-3 A Y A D I V M T Q S Q K F M S T S V G D

121 AGGGTCAGCG TCACCTGCAA GGCCAGTCAG AATGTGGGTA CTAATGTAGC CTGGTATCAA
TCCCAGTCGC AGTGGACGTT CCGGTCAGTC TTACACCCAT GATTACATCG GACCATAGTT
18 R V S V T C K A S O N V G T N V A W Y Q
* * * * *
CDR #1

181 CAGAAACCAG GGCAATCTCC TAAAGCACTG ATTTACTCGT CATCCTACCG GTACAGTGGA
GTCTTTGGTC CCGTTAGAGG ATTTCTGAC TAAATGAGCA GTAGGATGGC CATGTCACCT
38 Q K P G Q S P K A L I Y S S S Y R Y S G
* * * * *
CDR #2

241 GTCCCTGATC GCTTCACAGG CAGTGGATCT GGGACAGATT TCACTCTCAC CATCAGCCAT
CAGGGACTAG CGAAGTGTCC GTCACCTAGA CCCTGTCTAA AGTGAGAGTG GTAGTCGGTA
58 V P D R F T G S G S G T D F T L T I S H

301 GTGCAGTCTG AAGACTTGGC AGACTATTTC TGTCAGCAAT ATAACATCTA TCCTCTCACG
CACGTCAGAC TTCTGAACCG TCTGATAAAG ACAGTCGTTA TATTGTAGAT AGGAGAGTGC
78 V Q S E D L A D Y F C Q Q Y N I Y P L T
* * * * *
CDR #3

BstBI

361 TTCGGTCCTG GGACCAAGCT GGAGCTTCGA AGAGCTGTGG CTGCACCATC TGTCTTCATC
AAGCCAGGAC CCTGGTTCGA CCTCGAAGCT TCTCGACACC GACGTGGTAG ACAGAAGTAG
98 F G P G T K L E L R R A V A A P S V F I

421 TTCCCGCCAT CTGATGAGCA GTTGAAATCT GGAAGTCTT CTGTTGTGTG CCTGCTGAAT
AAGGGCGGTA GACTACTCGT CAACTTTAGA CCTTGACGAA GACAACACAC GGACGACTTA
118 F P P S D E Q L K S G T A S V V C L L N

481 AACTTCTATC CCAGAGAGGC CAAAGTACAG TGGAAGGTGG ATAACGCCCT CCAATCGGGT
TTGAAGATAG GGTCTCTCCG GTTTCATGTC ACCTTCCACC TATTGCGGGA GGTTAGCCCA
138 N F Y P R E A K V Q W K V D N A L Q S G

541 AACTCCCAGG AGAGTGTAC AGAGCAGGAC AGCAAGGACA GCACCTACAG CCTCAGCAGC
TTGAGGGTCC TCTCACAGTG TCTCGTCTCG TCGTTCCTGT CGTGGATGTC GGAGTCGTGC
158 N S Q E S V T E Q D S K D S T Y S L S S

601 ACCCTGACGC TGAGCAAAGC AGACTACGAG AAACACAAAG TCTACGCCTG CGAAGTCACC
TGGGACTGCG ACTCGTTTCG TCTGATGCTC TTTGTGTTTC AGATGCGGAC GCTTCAGTGG
178 T L T L S K A D Y E K H K V Y A C E V T

661 CATCAGGGCC TGAGCTCGCC CGTCACAAAG AGCTTCAACA GGGGAGAGTG
GTAGTCCCGG ACTCGAGCGG GCAGTGTTTC TCGAAGTTGT CCCCTCTCAC
198 H Q G L S S P V T K S F N R G E C

711 TTAA
AATT
216 O

FIG. 19



1 ATGAAAAGA ATATCGCATT TCTTCTTGCA TCTATGTTTCG TTTTTCCTAT TGCTACAAAC
TACTTTTTCT TATAGCGTAA AGAAGAACGT AGATACAAGC AAAAAAGATA ACGATGTTTG
-23 M K K N I A F L L A S M F V F S I A T N

61 GCGTACGCTG AGGTGCAGCT GGTGGAGTCT GGGGGAGGCT TAGTGCCGCC TGGAGGGTCC
CGCATGCGAC TCCACGTCGA CCACCTCAGA CCCCTCCGA ATCACGGCGG ACCTCCCAGG
-3 A Y A E V Q L V E S G G G L V P P G G S

121 CTGAAACTCT CCTGTGCAGC CTCTGGATTCT ATATTAGTA GTTATGGCAT GTCTTGGGTT
GACTTTGAGA GGACACGTCG GAGACCTAAG TATAAGTCAT CAATACCGTA CAGAACCCAA
18 L K L S C A A S G F I F S S Y G M S W V
* * * *

CDR #1

181 CGCCAGACTC CAGGCAAGAG CCTGGAGTTG GTCGCAACCA TTAATAATAA TGGTGATAGC
GCGGTCTGAG GTCCGTTCTC GGACCTCAAC CAGCGTTGGT AATTATTATT ACCACTATCG
38 R Q T P G K S L E L V A T I N N N G D S
* * * * *

241 ACCTATTATC CAGACAGTGT GAAGGGCCGA TTCACCATCT CCCGAGACAA TGCCAAGAAC
TGGATAATAG GTCTGTCACA CTTCCCGGCT AAGTGGTAGA GGGCTCTGTT ACGGTTCTTG
58 T Y Y P D S V K G R F T I S R D N A K N
* * * * *

CDR #2

301 ACCCTGTACC TGCAAATGAG CAGTCTGAAG TCTGAGGACA CAGCCATGTT TTAAGTGTGCA
TGGGACATGG ACGTTTACTC GTCAGACTTC AGACTCCTGT GTCGGTACAA AATGACACGT
78 T L Y L Q M S S L K S E D T A M F Y C A

361 AGAGCCCTCA TTAGTTCGGC TACTTGTTTT GGTACTGGG GCCAAGGGAC TCTGGTCACT
TCTCGGGAGT AATCAAGCCG ATGAACCAAA CCAATGACCC CGGTTCCCTG AGACCAAGTGA
98 R A L I S S A T W F G Y W G Q G T L V T
* * * * *

CDR #3

ApaI

421 GTCTCTGCAG CCTCCACCAA GGGCCCATCG GTCTTCCCCC TGGCACCCCTC CTCCAAGAGC
CAGAGACGTC GGAGGTGGTT CCCGGGTAGC CAGAAGGGGG ACCGTGGGAG GAGGTTCTCG
118 V S A A S T K G P S V F P L A P S S K S

481 ACCTCTGGGG GCACAGCGGC CCTGGGCTGC CTGGTCAAGG ACTACTTCCC CGAACCGGTG
TGGAGACCCC CGTGTGCGCCG GGACCCGACG GACCAGTTCC TGATGAAGGG GCTTGGCCAC
138 T S G G T A A L G C L V K D Y F P E P V

541 ACGGTGTCGT GGAAGTCAGG CGCCCTGACC AGCGGCGTGC ACACCTTCCC GGCTGTCCCTA
TGCCACAGCA CCTTGAGTCC GCGGGACTGG TCGCCGCACG TGTGGAAGGG CCGACAGGAT
158 T V S W N S G A L T S G V H T F P A V L

601 CAGTCCTCAG GACTCTACTC CCTCAGCAGC GTGGTGACCG TGCCCTCCAG CAGCTTGGGC
GTCAGGAGTC CTGAGATGAG GGAGTCGTCG CACCAGTGGC ACGGGAGGTC GTCGAACCCG
178 Q S S G L Y S L S S V V T V P S S S L G

FIG. 20A



661 ACCCAGACCT ACATCTGCAA CGTGAATCAC AAGCCCAGCA ACACCAAGGT GGACAAGAAA
TGGGTCTGGA TGTAGACGTT GCACTTAGTG TTCGGGTCGT TGTGGTTCCA CCTGTTCTTT
198 T Q T Y I C N V N H K P S N T K V D K K

721 GTTGAGCCCA AATCTTGTGA CAAAACAC ACATGA
CAACTCGGGT TTAGAACACT GTTTTGAGTG TGTACT
218 V E P K S C D K T H T O

FIG. 20B



Light Chain Primers:

MKLC-1, 22mer

5' CAGTCCAACCTGTTTCAGGACGCC 3'

MKLC-2, 22mer

5' GTGCTGCTCATGCTGTAGGTGC 3'

MKLC-3, 23mer

5' GAAGTTGATGTCTTGTGAGTGGC 3'

Heavy Chain Primers:

IGG2AC-1, 24mer

5' GCATCCTAGAGTCACCGAGGAGCC 3'

IGG2AC-2, 22mer

5' CACTGGCTCAGGGAAATAACCC 3'

IGG2AC-3, 22mer

5' GGAGAGCTGGGAAGGTGTGCAC 3'

FIG. 21



Light chain forward primer

6G4.light.Nsi 36-MER

5' CCAATGCATACGCT GAC ATC GTG ATG ACC CAG ACC CC 3'
 T T T T
 A A

Light chain reverse primer

6G4.light.Mun 35-MER

5' AGA TGT CAA TTG CTC ACT GGA TGG TGG GAA GAT GG 3'

FIG. 22



Heavy chain forward primer

6G4.heavy.Mlu 32-MER

5' CAAACGCGTACGCT GAG ATC CAG CTG CAG CAG 3'
 T C

Heavy chain reverse primer

SL002B 39-MER

5' CGATGGGCCCCG ATAGACCGATGGGGCTGTTGTTTGGC 3'
 T
 A
 G

FIG. 23



70 G ATATCGTGAT GACACAGACA CCACTCTCCC TGCCTGTCAG TCTTGAGAT
C TATAGCACTA CTGTGTCTGT GGTGAGAGGG ACGGACAGTC AGAACCTCTA
1 D I V M T Q T P L S L P V S L G D

121 CAGGCCTCCA TCTCTTGCAG ATCTAGTCAG AGCCTTGTAC ACGGTATTGG AAACACCTAT
GTCCGGAGGT AGAGAACGTC TAGATCAGTC TCGGAACATG TGCCATAACC TTTGTGGATA
18 Q A S I S C R S S O S L V H G I G N T Y
* * * * * * * * * * * * * *

CDR #1

181 TTACATTGGT ACCTGCAGAA GCCAGGCCAG TCTCCAAAGC TCCTGATCTA CAAAGTTTCC
AATGTAACCA TGGACGTCTT CCGTCCGGTC AGAGGTTTCG AGGACTAGAT GTTTCAAAGG
38 L H W Y L Q K P G Q S P K L L I Y K V S
* * * * * * * * *

CDR #2

241 AACCGATTTT CTGGGGTCCC AGACAGGTTT AGTGGCAGTG GATCAGGGAC AGATTTTACA
TTGGCTAAAA GACCCAGGG TCTGTCCAAG TCACCGTCAC CTAGTCCCTG TCTAAAGTGT
58 N R F S G V P D R F S G S G S G T D F T
* * * * *

301 CTCAGGATCA GCAGAGTGGA GGCTGAGGAT CTGGGACTTT ATTTCTGCTC TCAAAGTACA
GAGTCCTAGT CGTCTCACCT CCGACTCCTA GACCCTGAAA TAAAGACGAG AGTTTCATGT
78 L R I S R V E A E D L G L Y F C S Q S T
* * * * *

CDR #3

361 CATGTTCCGC TCACGTTCCG TGCTGGGACC AAGCTGGAGC TGAAACGGGC TGATGCTGCA
GTACAAGGCG AGTGCAAGCC ACGACCCTGG TTCGACCTCG ACTTTGCCCG ACTACGACGT
98 H V P L T F G A G T K L E L K R A D A A
* * * * *

MunI

421 CCAACTGTAT CCATCTTCCC ACCATCCAGT GAGCAATTGA
GGTTGACATA GGTAGAAGGG TGGTAGGTCA CTCGTTAAC T
118 P T V S I F P P S S E Q L K

FIG. 24



70 G AGATTCAGCT GCAGCAGTCT GGACCTGAGC TGATGAAGCC TGGGGCTTCA
C TCTAAGTCGA CGTCGTCAGA CCTGGACTCG ACTACTTCGG ACCCCGAAGT
1 E I Q L Q Q S G P E L M K P G A S

121 GTGAAGATAT CCTGCAAGGC TTCTGGTTAT TCATTCAGTA GCCACTACAT GCACTGGGTG
CACTTCTATA GGACGTTCCG AAGACCAATA AGTAAGTCAT CGGTGATGTA CGTGACCCAC
18 V K I S C K A S G Y S F S S H Y M H W V
* * * * *

CDR #1

181 AAGCAGAGCC ATGGAAAGAG CCTTGAGTGG ATTGGCTACA TTGATCCTTC CAATGGTGAA
TTCGTCTCGG TACCTTTCTC GGAAGTCACC TAACCGATGT AACTAGGAAG GTTACCACCT
38 K Q S H G K S L E W I G Y I D P S N G E
* * * * *

CDR #2

241 ACTACTTACA ACCAGAAATT CAAGGGCAAG GCCACATTGA CTGTAGACAC ATCTTCCAGC
TGATGAATGT TGGTCTTTAA GTTCCCGTTC CGGTGTAAGT GACATCTGTG TAGAAGGTCG
58 T T Y N Q K F K G K A T L T V D T S S S
* * * * *

301 ACAGCCAACG TGCATCTCAG CAGCCTGACA TCTGATGACT CTGCAGTCTA TTTCTGTGCA
TGTCGGTTGC ACGTAGAGTC GTCGGACTGT AGACTACTGA GACGTCAGAT AAAGACACGT
78 T A N V H L S S L T S D D S A V Y F C A

361 AGAGGGGACT ATAGATACAA CGGCGACTGG TTTTTCGATG TCTGGGGCGC AGGGACCACG
TCTCCCCTGA TATCTATGTT GCCGCTGACC AAAAAGCTAC AGACCCCGCG TCCCTGGTGC
98 R G D Y R Y N G D W F F D V W G A G T T
* * * * *

CDR #3

BstEII ApaI

421 GTCACCGTCT CCTCCGCCAA AACCGACAGC CCCATCGGTC TATCCGGGCC
CAGTGGCAGA GGAGGCGGAT TTGGCTGTCG GGGTAGCCAG ATAGGCCCGG
118 V T V S S A K T D S P I G L S G P

471 CATC
GTAG
135 I

FIG. 25



5' CTTGGTGGAGGCGGAGGAGACG 3'

Mutagenesis Primer for 6G425VL

DS/VF 38MER

5' GAAACGGGCTGTTGCTGCACCAACTGTATTCATCTTCC 3'

SYN.BstEII 31 MER

5' GTCACCGTCT CCTCCGCCTC CACCAAGGGC C 3'

SYN.Apa 22 MER

5' CTTGGTGGAGGCGGAGGAGACG 3'

FIG. 26



1 ATGAAGAAGA ATATCGCATT TCTTCTTGCA TCTATGTTTCG TTTTCTCTAT TGCTACAAAT
TACTTCTTCT TATAGCGTAA AGAAGAACGT AGATACAAGC AAAAAAGATA ACGATGTTTA
-23 M K K N I A F L L A S M F V F S I A T N

61 GCATACGCTG ATATCGTGAT GACACAGACA CCACTCTCCC TGCCTGTCAG TCTTGGAGAT
CGTATGCGAC TATAGCACTA CTGTGTCTGT GGTGAGAGGG ACGGACAGTC AGAACCTCTA
-3 A Y A D I V M T Q T P L S L P V S L G D

121 CAGGCCTCCA TCTCTTGCGAG ATCTAGTCAG AGCCTTGTTAC ACGGTATTGG AAACACCTAT
GTCCGGAGGT AGAGAACGTC TAGATCAGTC TCGGAACATG TGCCATAACC TTTGTGGATA
18 Q A S I S C R S S O S L V H G I G N T Y
* * * * * * * * * * * * * * *

CDR #1

181 TTACATTGGT ACCTGCAGAA GCCAGGCCAG TCTCCAAAGC TCCTGATCTA CAAAGTTTCC
AATGTAACCA TGGACGTCTT CCGTCCGGTC AGAGGTTTCG AGGACTAGAT GTTTCAAAGG
38 L H W Y L Q K P G Q S P K L L I Y K V S
* * * * * * * * *

CDR #2

241 AACCGATTTT CTGGGGTCCC AGACAGGTTT AGTGGCAGTG GATCAGGGAC AGATTTTACA
TTGGCTAAAA GACCCAGGG TCTGTCCAAG TCACCGTCAC CTAGTCCCTG TCTAAAGTGT
58 N R F S G V P D R F S G S G S G T D F T
* * * * *

301 CTCAGGATCA GCAGAGTGGA GGCTGAGGAT CTGGGACTTT ATTTCTGCTC TCAAAGTACA
GAGTCCTAGT CGTCTCACCT CCGACTCCTA GACCCTGAAA TAAAGACGAG AGTTTCATGT
78 L R I S R V E A E D L G L Y F C S Q S T
* * * * *

CDR #3

361 CATGTTCCGC TCACGTTCCG TGCTGGGACC AAGCTGGAGC TGAAACGGGC TGTGCTGCA
GTACAAGGCG AGTGCAAGCC ACGACCCTGG TTCGACCTCG ACTTTGCCCG ACAACGACGT
98 H V P L T F G A G T K L E L K R A V A A
* * * * *

421 CCAACTGTAT TCATCTTCCC ACCATCCAGT GAGCAATTGA AATCTGGAAC TGCCTCTGTT
GGTTGACATA AGTAGAAGGG TGGTAGGTCA CTCGTAACT TTAGACCTTG ACGGAGACAA
118 P T V F I F P P S S E Q L K S G T A S V

481 GTGTGCCTGC TGAATAACTT CTATCCCAGA GAGGCCAAAG TACAGTGGAA GGTGGATAAC
CACACGGACG ACTTATTGAA GATAGGGTCT CTCCGGTTTC ATGTACACCTT CCACCTATTG
138 V C L L N N F Y P R E A K V Q W K V D N

541 GCCCTCCAAT CGGGTAACTC CCAGGAGAGT GTCACAGAGC AGGACAGCAA GGACAGCACC
CGGGAGGTTA GCCCATTGAG GGTCTCTCA CAGTGTCTCG TCCTGTCTGT CCTGTCTGTG
158 A L Q S G N S Q E S V T E Q D S K D S T

601 TACAGCCTCA GCAGCACCCT GACGCTGAGC AAAGCAGACT ACGAGAAACA CAAAGTCTAC
ATGTCGGAGT CGTCGTGGGA CTGCGACTCG TTTCTGTCTGA TGCTCTTTGT GTTTCAGATG
178 Y S L S S T L T L S K A D Y E K H K V Y

FIG. 27A



661 GCCTGCGAAG TCACCCATCA GGGCCTGAGC TCGCCCGTCA CAAAGAGCTT CAACAGGGGA
CGGACGCTTC AGTGGGTAGT CCCGACTCG AGCGGCAGT GTTCTCGAA GTTGTCCTT
198 A C E V T H Q G L S S P V T K S F N R G

721 GAGTGTAA
CTCACAATT
218 E C O

FIG. 27B



1 ATGAAAAAGA ATATCGCATT TCTTCTTGCA TCTATGTTTCG TTTTCTCTAT TGCTACAAAC
 TACTTTTTTCT TATAGCGTAA AGAAGAACGT AGATACAAGC AAAAAAGATA ACGATGTTTG
 -23 M K K N I A F L L A S M F V F S I A T N

 61 GCGTACGCTG AGATTTCAGCT GCAGCAGTCT GGACCTGAGC TGATGAAGCC TGGGGCTTCA
 CGCATGCGAC TCTAAGTCGA CGTCGTCAGA CCTGGACTCG ACTACTTCGG ACCCCGAAGT
 -3 A Y A E I Q L Q Q S G P E L M K P G A S

 121 GTGAAGATAT CCTGCAAGGC TTCTGGTTAT TCATTTCAGTA GCCACTACAT GCACTGGGTG
 CACTTCTATA GGACGTTCCG AAGACCAATA AGTAAGTCAT CGGTGATGTA CGTGACCCAC
 18 V K I S C K A S G Y S F S S H Y M H W V
 * * * * *

CDR #1

181 AAGCAGAGCC ATGGAAAGAG CCTTGAGTGG ATTGGCTACA TTGATCCTTC CAATGGTGAA
 TTCGTCTCGG TACCTTCTC GGAACTCACC TAACCGATGT AACTAGGAAG GTTACCACTT
 38 K Q S H G K S L E W I G Y I D P S N G E
 * * * * *

CDR #2

241 ACTACTTACA ACCAGAAATT CAAGGGCAAG GCCACATTGA CTGTAGACAC ATCTTCCAGC
 TGATGAATGT TGGTCTTTAA GTTCCCGTTC CGGTGTAAC TACATCTGTG TAGAAGGTCG
 58 T T Y N Q K F K G K A T L T V D T S S S
 * * * * *

301 ACAGCCAACG TGCATCTCAG CAGCCTGACA TCTGATGACT CTGCAGTCTA TTTCTGTGCA
 TGTCGGTTGC ACGTAGAGTC GTCGGACTGT AGACTACTGA GACGTCAGAT AAAGACACGT
 78 T A N V H L S S L T S D D S A V Y F C A

361 AGAGGGGACT ATAGATACAA CGGCGACTGG TTTTTCGATG TCTGGGGCGC AGGGACCACG
 TCTCCCCTGA TATCTATGTT GCCGCTGACC AAAAAGCTAC AGACCCCGCG TCCCTGGTGC
 98 R G D Y R Y N G D W F F D V W G A G T T
 * * * * *

CDR #3

421 GTCACCGTCT CCTCCGCCTC CACCAAGGGC CCATCGGTCT TCCCCCTGGC ACCCTCCTCC
 CAGTGGCAGA GGAGGCGGAG GTGGTTCCCG GGTAGCCAGA AGGGGGACCG TGGGAGGAGG
 118 V T V S S A S T K G P S V F P L A P S S

481 AAGAGCACCT CTGGGGGCAC AGCGGCCCTG GGCTGCCTGG TCAAGGACTA CTTCCCCGAA
 TTCTCGTGGA GACCCCGTG TCGCCGGGAC CCGACGGACC AGTTCTGAT GAAGGGGCTT
 138 K S T S G G T A A L G C L V K D Y F P E

541 CCGGTGACGG TGTCGTGGAA CTCAGGCGCC CTGACCAGCG GCGTGCACAC CTTCCCGGCT
 GGCCACTGCC ACAGCACCTT GAGTCCGCGG GACTGGTCGC CGCACGTGTG GAAGGGCCGA
 158 P V T V S W N S G A L T S G V H T F P A

601 GTCCTACAGT CCTCAGGACT CTACTCCCTC AGCAGCGTGG TGACCGTGCC CTCCAGCAGC
 CAGGATGTCA GGAGTCCTGA GATGAGGGAG TCGTCGCACC ACTGGCACGG GAGGTCGTCG
 178 V L Q S S G L Y S L S S V V T V P S S S

FIG. 28A



661 TTGGGCACCC AGACCTACAT CTGCAACGTG AATCACAAGC CCAGCAACAC CAAGGTGGAC
AACCCTGGG TCTGGATGTA GACGTTGCAC TTAGTGTTCG GGTGTTGTG GTTCCACCTG
198 L G T Q T Y I C N V N H K P S N T K V D
721 AAGAAAGTTG AGCCCAATC TTGTGACAAA ACTCACACAT GA
TTCTTTCAAC TCGGGTTTAG AACACTGTTT TGAGTGTGTA CT
218 K K V E P K S C D K T H T O

FIG. 28B



Variable Light Chain Domain

	10	20	abcde	30	40
6G425	DIVMTQTPLSLPVS LGDQASISCRSSQSLVHGIGNTYLHWYLQKPGQSPKLLIY				
	#	#	#	#	#
F(ab)-1	DIQMTQSPSSLSASVGDRVTITCRSSQSLVHGIGNTYLHWYQQKPGKAPKLLIY				
	#	#	#	#	#
humkI	DIQMTQSPSSLSASVGDRVTITCRASKTI-----SKYLAWYQQKPGKAPKLLIY				
	=====				
	+++++				
	L1				

	50	60	70	80	90	100
6G425	YKVSNRFGV PDRFSDSGSGTDFTLRISRVEAEDLGLYFCSQSTHVPLTFGAGTKLELKR					
	#	#	#	#	#	#
F(ab)-1	YKVSNRFGVPSRFSGSGSGTDFTLTISLQPEDFATYYCSQSTHVPLTFGQGTKVEIKR					
	#	#	#	#	#	#
humkI	YSGSTLES GVP SRFSGSGSGTDFTLTISLQPEDFATYYCQHNEYPLTFGQGTKVEIKR					
	==			=====		
	+++++			+++++		
	L2			L3		

Variable Heavy Chain Domain

	10	20	30	40
6G425	EIQLQQSGPELMKPGASVKISCKASGYSFSSHYMHVWKQSHGKSLEWI			
	#	#	#	#
F(ab)-1	EVQLVESGGGLVQPGGSLRLSCAASGYSFSSHYMHVWRQAPGKGLEWV			
	#	#	#	#
humIII	EVQLVESGGGLVQPGGSLRLSCAASGFSFTGHWMNVWRQAPGKGLEWV			
	=====			
	+++++			
	H1			

	50	a	70	80	abc	90	100	110
6G425	GYIDPSNGETTYNQKFKGKATLTVDTSSTANVHLSSLTSDDSAVYFCAARGDYRYNGDWFFDVWGAGT							
	#	#	#	#	#	#	#	#
F(ab)-1	GYIDPSNGETTYNQKFKGRFTISRDN SKNTLYLQMNSLRAEDTAVYYCAARGDYRYNGDWFFDVWGQGT							
	#	#	#	#	#	#	#	#
humIII	GMIHPSDSETRYADSVKGRFTISRDN SKNTLYLQMNSLRAEDTAVYYCAARGIIFY-GTTYFDYWQGT							
	=====				=====			
	+++++				+++++			
	H2				H3			

FIG. 29

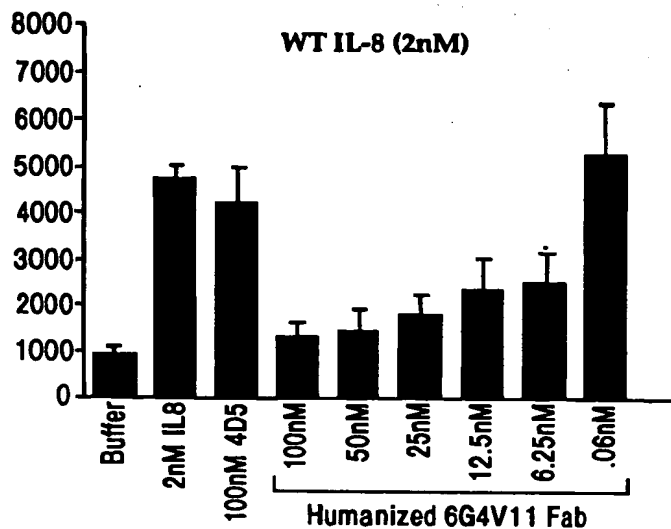


FIG. 30A

IC₅₀~12nM

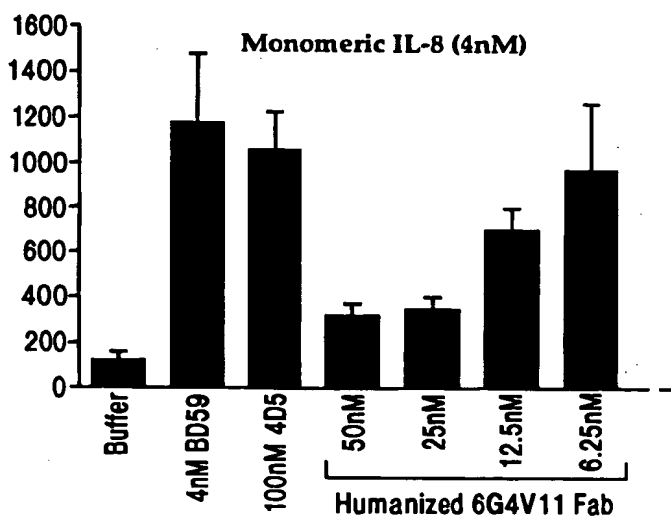


FIG. 30B

IC₅₀~15nM

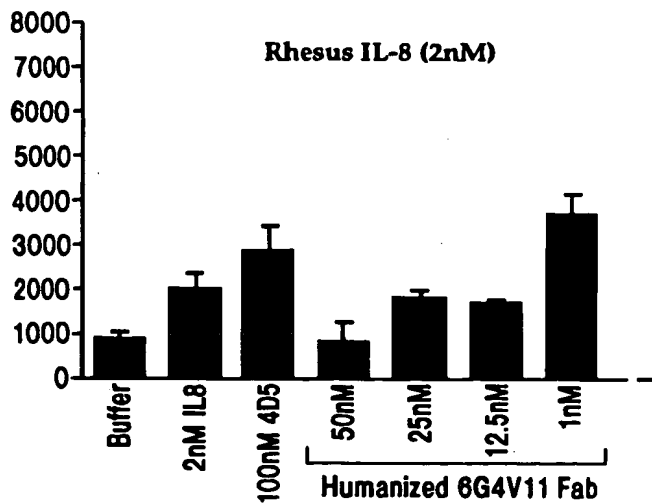


FIG. 30C

IC₅₀~22nM



Amino Acid Sequence of the humanized anti-IL-8 6G4.2.5V11 Light Chain

MKKNIAFLLASMFVFSIATNAYADIQMTQSPSSLSASVGDRTTITCRSSQSLVHGIGNTY
LHWYQQKPGKAPKLLIYKVSNNRFSGVPSRFSGSGGTDFTLTISSLQPEDFATYYCSQST
HVP LTFGQGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASVCLLNNFYPREAKVQWKVDN
ALQSGNSQESVTEQDSKDSSTLSLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRG
EC

Amino Acid Sequence of the humanized anti-IL-8 6G4.2.5V11 Heavy Chain

MKKNIAFLLASMFVFSIATNAYAEVLVQSGGGLVQPGGSLRLSCAASGYFSSHYMH
WVRQAPGKGLEWVG YIDPSNGETTYNQKFKGRFTLSRDNSKNTAYLQMNSLRAEDTAVYY
CARGDYRYNGDWFFDWGQGT LVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYF
PEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVTVTPSSSLGTQTYICNVNHHKPSNTK
VDKKVEPKSCDKTHT

Amino Acid Sequence of the peptide linker and M13 Phage Coat (gene-III)

SGGGSGGDFDYKMANANKGAMTENADENALQSDAKGKLDVATDYGAIDFIGDVVS
GLANGNGATGDFAGSSNSQMAQVGDGDN SPLMNNFRQYLP LPSLPQSV ECRPFVFSAGKPY
EFSIDCDKINLFRGVFAFLLYVATFMYVFTFANILRNKES

FIG. 31A



1 ATGAAAAAGA ATATCGCATT TCTTCTTGCA TCTATGTTTCG TTTTCTCTAT TGCTACAAAC
TACTTTTTCT TATAGCGTAA AGAAGAACGT AGATACAAGC AAAAAAGATA ACGATGTTTG
-23 M K K N I A F L L A S M F V F S I A T N

61 GCATACGCTG ATATCCAGAT GACCCAGTCC CCGAGCTCCC TGTCCGCCTC TGTGGGCGAT
CGTATGCGAC TATAGGTCTA CTGGGTCAGG GGCTCGAGGG ACAGGCGGAG ACACCCGCTA
-3 A Y A D I Q M T Q S P S S L S A S V G D

121 AGGGTCACCA TCACCTGCAG GTCAAGTCAA AGCTTAGTAC ATGGTATAGG TAACACGTAT
TCCCAGTGGT AGTGGACGTC CAGTTCAGTT TCGAATCATG TACCATATCC ACGATGCATA
18 R V T I T C R S S Q S L V H G I G N T Y

181 TTACACTGGT ATCAACAGAA ACCAGGAAAA GCTCCGAAAC TACTGATTTA CAAAGTATCC
AATGTGACCA TAGTTGTCTT TGGTCCTTTT CGAGGCTTTG ATGACTAAAT GTTTCATAGG
38 L H W Y Q Q K P G K A P K L L I Y K V S

241 AATCGATTCT CTGGAGTCCC TTCTCGCTTC TCTGGATCCG GTTCTGGGAC GGATTTTCACT
TTAGCTAAGA GACCTCAGGG AAGAGCGAAG AGACCTAGGC CAAGACCCCTG CCTAAAGTGA
58 N R F S G V P S R F S G S G S G T D F T

301 CTGACCATCA GCAGTCTGCA GCCAGAAGAC TTCGCAACTT ATTACTGTTC ACAGAGTACT
GACTGGTAGT CGTCAGACGT CGGTCTTCTG AAGCGTTGAA TAATGACAAG TGTCTCATGA
78 L T I S S L Q P E D F A T Y Y C S Q S T

361 CATGTCCCGC TCACGTTTGG ACAGGGTACC AAGGTGGAGA TCAAACGAAC TGTGGCTGCA
GTACAGGGCG AGTGCAAACC TGTCCTCATGG TTCCACCTCT AGTTTGCTTG ACACCGACGT
98 H V P L T F G Q G T K V E I K R T V A A

421 CCATCTGTCT TCATCTTCCC GCCATCTGAT GAGCAGTTGA AATCTGGAAC TGCTTCTGTT
GGTAGACAGA AGTAGAAGGG CGGTAGACTA CTCGTCAACT TTAGACCTTG ACGAAGACAA
118 P S V F I F P P S D E Q L K S G T A S V

481 GTGTGCCTGC TGAATAACTT CTATCCCAGA GAGGCCAAAG TACAGTGGA GGTGGATAAC
CACACGGACG ACTTATTGAA GATAGGGTCT CTCCGGTTTC ATGTCACCTT CCACCTATTG
138 V C L L N N F Y P R E A K V Q W K V D N

541 GCCCTCCAAT CGGGTAACTC CCAGGAGAGT GTCACAGAGC AGGACAGCAA GGACAGCACC
CGGGAGGTTA GCCCATTGAG GGTCTCTCTCA CAGTGTCTCG TCCTGTCGTT CCTGTCGTGG
158 A L Q S G N S Q E S V T E Q D S K D S T

601 TACAGCCTCA GCAGCACCCCT GACGCTGAGC AAAGCAGACT ACGAGAAACA CAAAGTCTAC
ATGTCGGAGT CGTCGTGGGA CTGCGACTCG TTTCGTCTGA TGCTCTTTGT GTTTCAGATG
178 Y S L S S T L T L S K A D Y E K H K V Y

661 GCCTGCGAAG TCACCCATCA GGGCCTGAGC TCGCCCGTCA CAAAGAGCTT CAACAGGGGA
CGGACGCTTC AGTGGGTAGT CCCGGAAGTC AGCGGGCAGT GTTCTCTGAA GTTGTCCCCT
198 A C E V T H Q G L S S P V T K S F N R G

721 GAGTGTTAAG CTGATCCTCT ACGCCGGACG CATCGTGGCC CTAGTACGCA ACTAGTCGTA
CTCACAATTC GACTAGGAGA TCGGGCCTGC GTAGCACCGG GATCATGCGT TGATCAGCAT
218 E C O

FIG. 31B



Amino Acid Sequence of the humanized anti-IL-8 6G4.2.5V19 Light Chain

MKKNIAFLLASMFVFSIATNAYADIQMTQSPSSLSASVGDRTTITCRSSQSLVHGIGNTY
LHWYQQKPGKAPKLLIYKVSNRFSGVPSRFSGSGGTDFTLTISLQPEDFATVYCSQST
HVPLTFGQGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASVVCCLNNFYPREAKVQWKVDN
ALQSGNSQESVTEQDSKDSSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRG
EC

Amino Acid Sequence of the humanized anti-IL-8 6G4.2.5V19 Heavy Chain

MKKNIAFLLASMFVFSIATNAYAEVQLVESGGGLVQPGGSLRLSCAASGYSFSSHYMH
WVKQAPGKGLEWVGYIDPSNGETTYNQFKGRFTLSRDNSKNTAYLQMNSLRAEDTAVYY
CARGDYRYNGDWFFDVWGQGTLLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYF
PEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVTVPSSSLGTQTYICNVNHKPSNTK
VDKKVEPKSCDKTHT

FIG. 31C

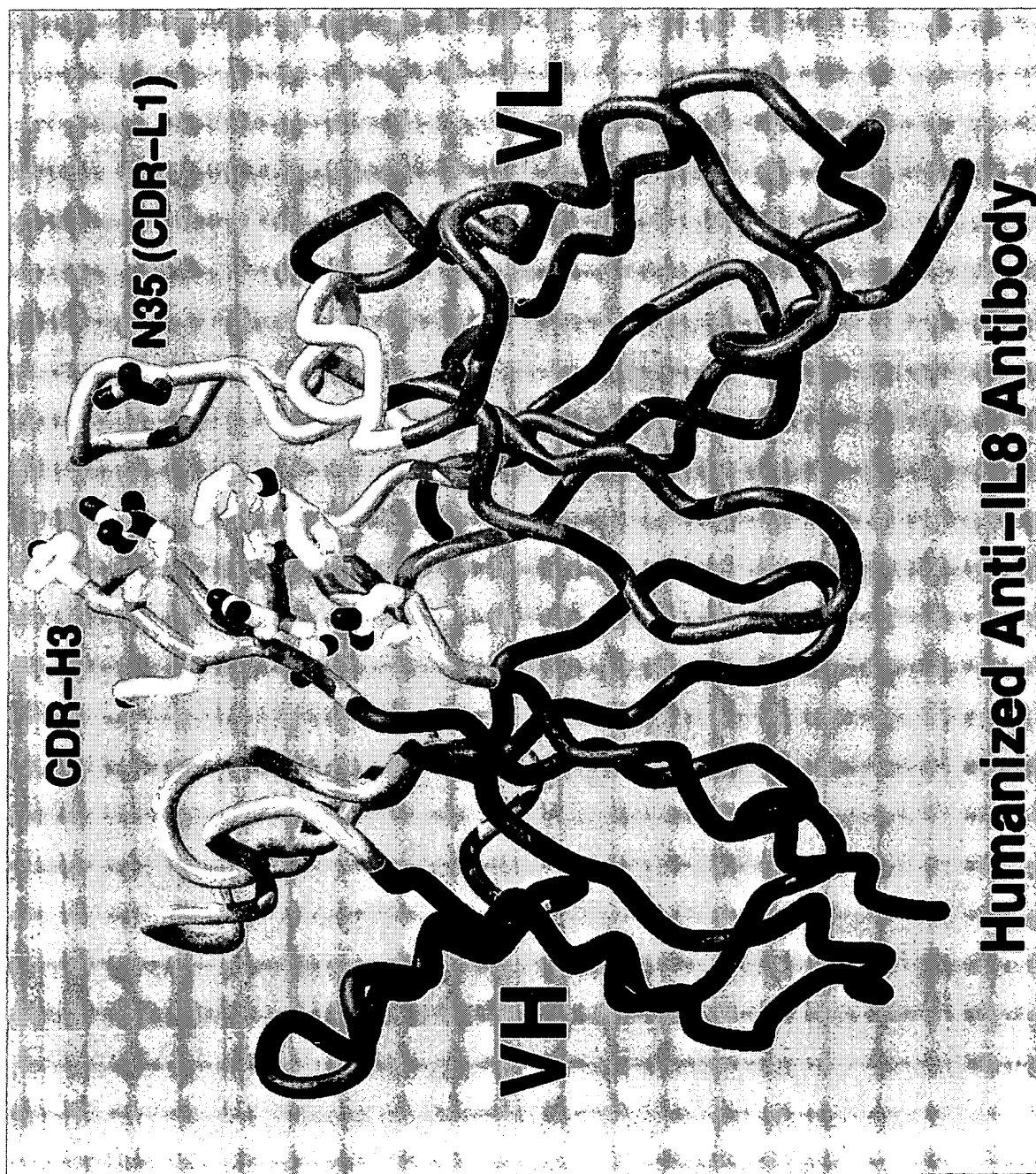


FIG. 32

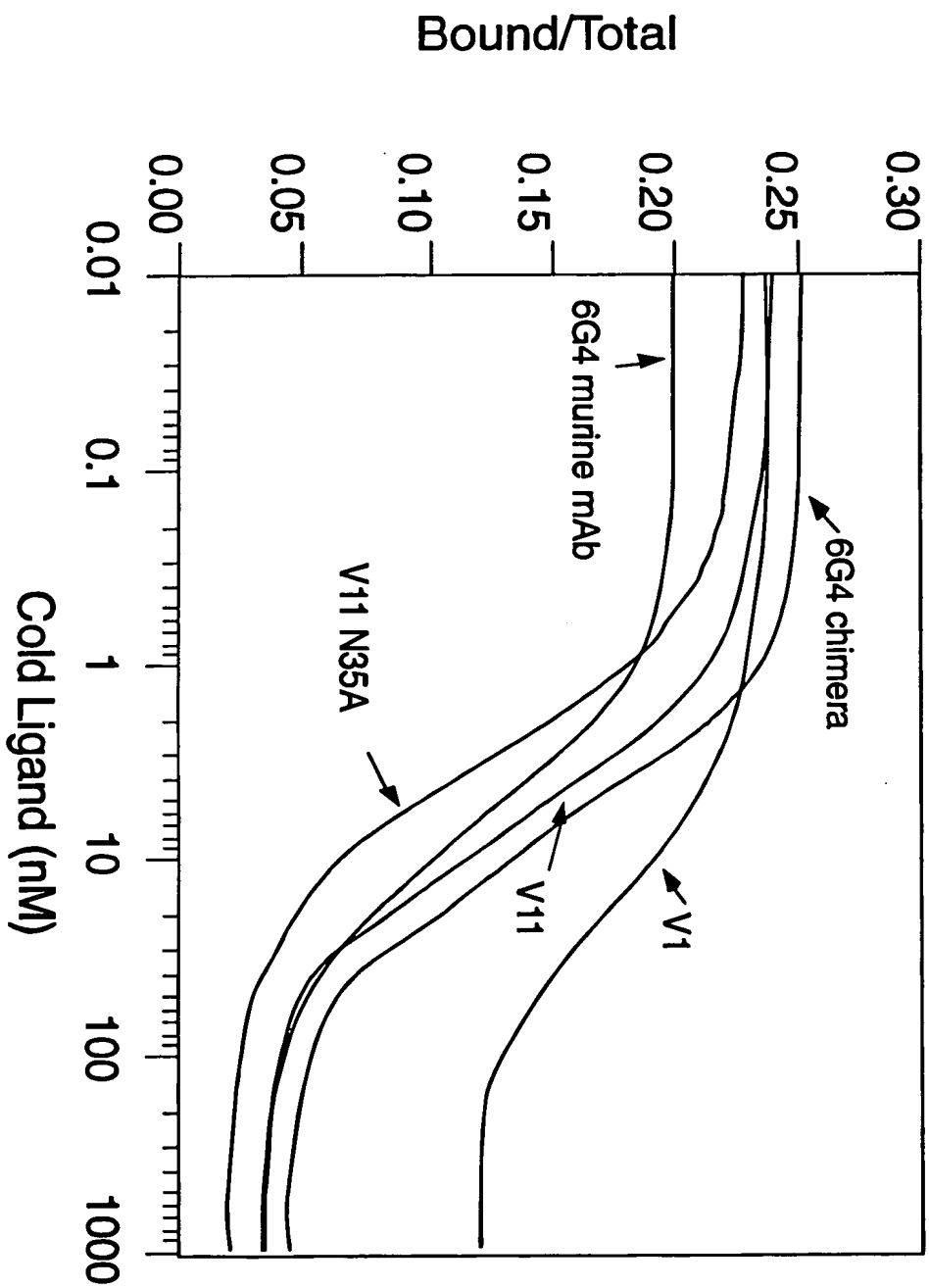


FIG. 33

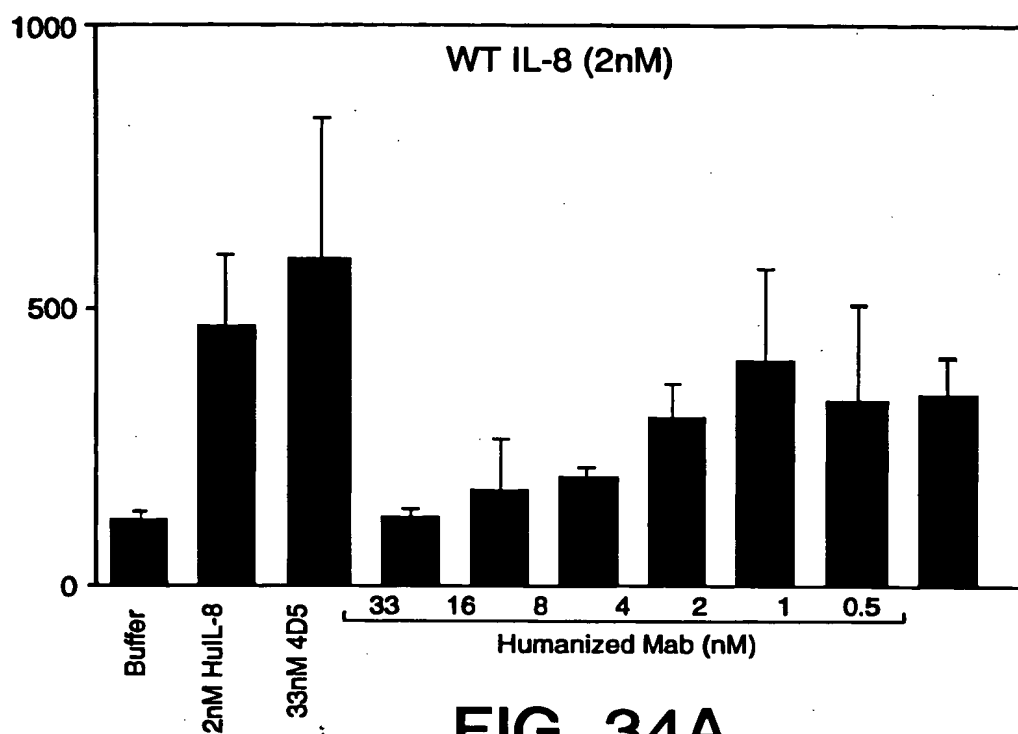


FIG. 34A

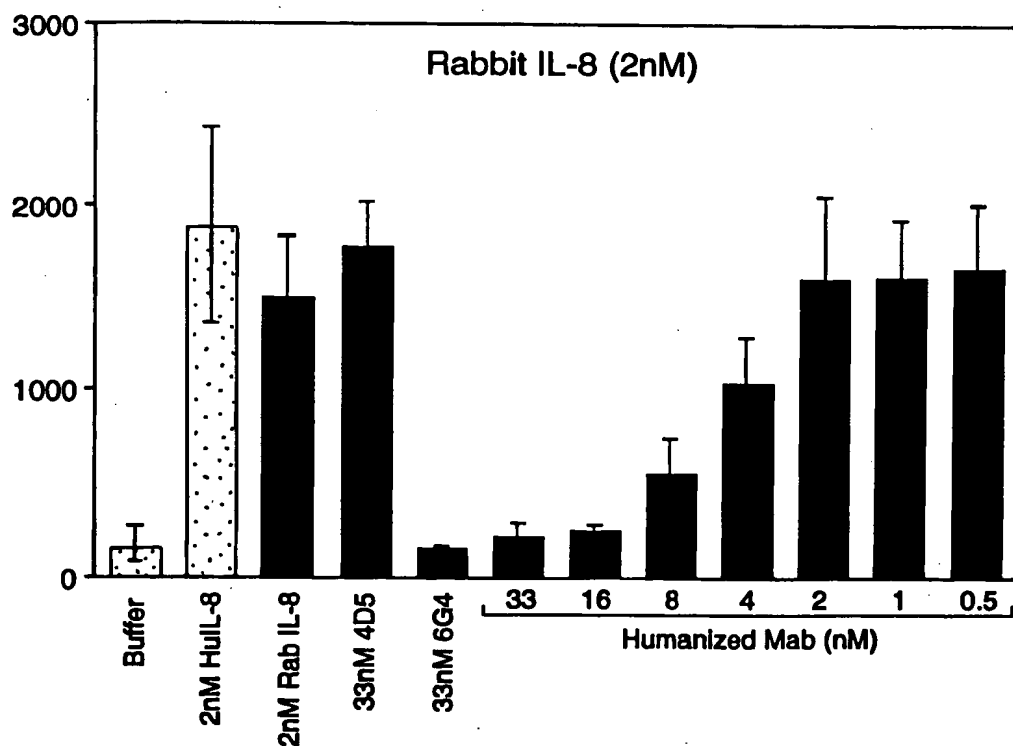


FIG. 34B

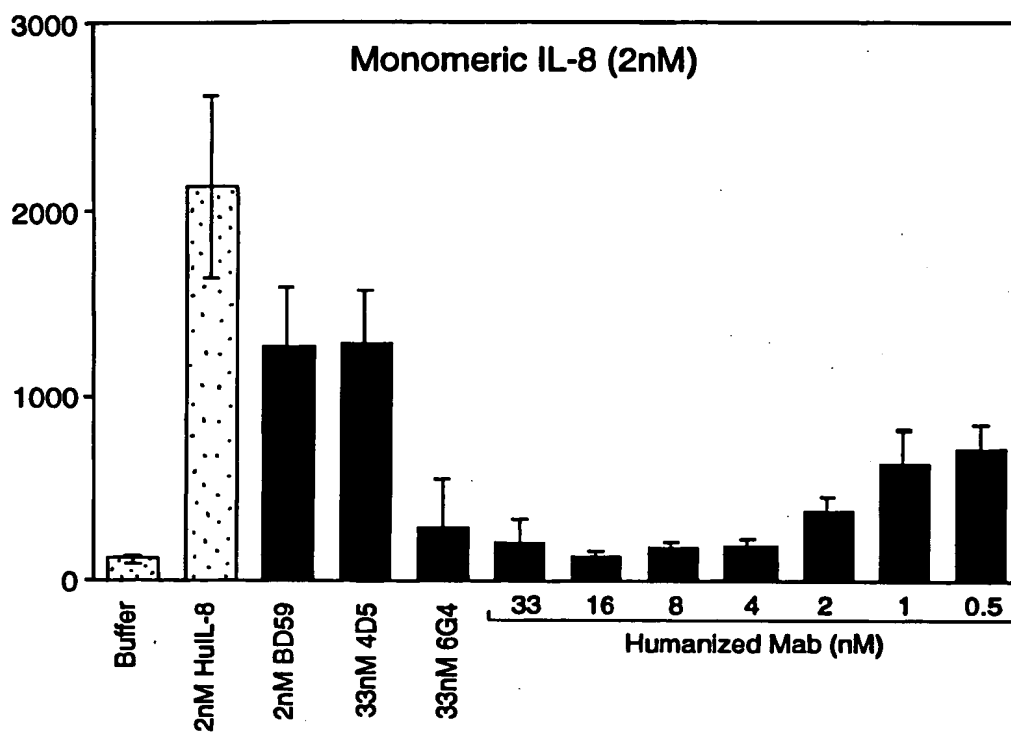


FIG. 34C

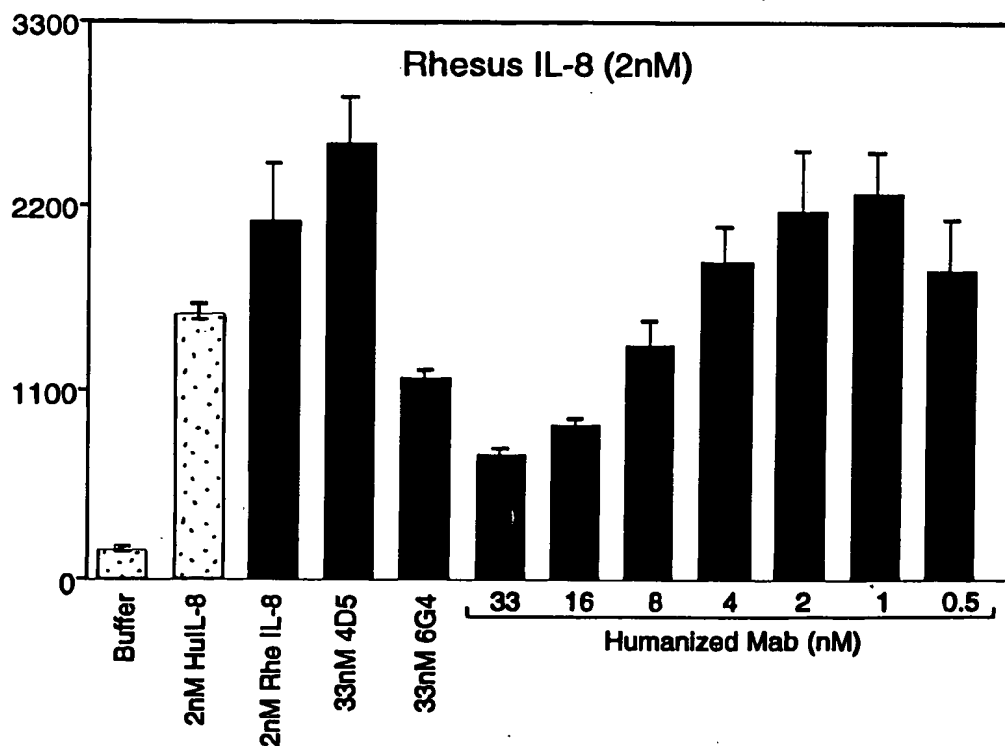


FIG. 34D



Amino Acid Sequence of the humanized anti-IL-8 6G4.2.5V11N35A Light Chain

MKKNIAFL¹LLASMFVFSIATNAYADIQMTQSPSSLSASVGDRTTITCRSSQSLVHGIGATY
LHWYQQKPGKAPKLLIYKVSNRFSGVPSRFSGSGGTDFLTITISLQPEDFATYYCSQST
HVPLTFGQGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDN
ALQSGNSQESVTEQDSKDS²TYSLSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRG
EC

Amino Acid Sequence of the humanized anti-IL-8 6G4.2.5V11N35A Heavy Chain

MKKNIAFL¹LLASMFVFSIATNAYAEVQLVQSGGGLVQPGGSLRLSCAASGYSFSSHYMH
WVRQAPGKGLEWVG²YIDPSNGETTYNQKFGRFTLSRDNSKNTAYLQMNSLRAEDTAVYY
CARGDYRYNGDWFFDVWGQGT³LVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYF
PEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVTVTPSSSLGTQTYICNVNHKPSNTK
VDKKVEPKSCDK⁴THT

Amino Acid Sequence of the putative Pepsin Cleavage Site and GCN4 Leucine Zipper

CPPCPAPELLGGRMKQLEDKVEELLSKNYHLENEVARLKKLVGER

FIG. 35



1 ATGAAAAAGA ATATCGCATT TCTTCTTGCA TCTATGTTTCG TTTTCTCTAT TGCTACAAAC
TACTTTTCT TATAGCGTAA AGAAGAACGT AGATACAAGC AAAAAAGATA ACGATGTTTG
-23 M K K N I A F L L A S M F V F S I A T N

61 GCATACGCTG ATATCCAGAT GACCCAGTCC CCGAGCTCCC TGTCCGCCTC TGTGGGCGAT
CGTATGCGAC TATAGGTCTA CTGGGTGAGG GGCTCGAGGG ACAGGCGGAG ACACCCGCTA
-3 A Y A D I Q M T Q S P S S L S A S V G D

121 AGGGTCACCA TCACCTGCAG GTCAAGTCAA AGCTTAGTAC ATGGTATAGG TGCTACGTAT
TCCCAGTGGT AGTGGACGTC CAGTTCAGTT TCGAATCATG TACCATATCC ACGATGCATA
18 R V T I T C R S S O S L V H G I G A T Y

181 TTACACTGGT ATCAACAGAA ACCAGGAAAA GCTCCGAAAC TACTGATTTA CAAAGTATCC
AATGTGACCA TAGTTGTCTT TGGTCCTTTT CGAGGCTTTG ATGACTAAAT GTTTCATAGG
38 L H W Y Q Q K P G K A P K L L I Y K V S

241 AATCGATTCT CTGGAGTCCC TTCTCGCTTC TCTGGATCCG GTTCTGGGAC GGATTTTCACT
TTAGCTAAGA GACCTCAGGG AAGAGCGAAG AGACCTAGGC CAAGACCCTG CCTAAAGTGA
58 N R F S G V P S R F S G S G S G T D F T

301 CTGACCATCA GCAGTCTGCA GCCAGAAGAC TTCGCAACTT ATTACTGTTC ACAGAGTACT
GACTGGTAGT CGTCAGACGT CGGTCTTCTG AAGCGTTGAA TAATGACAAG TGTCTCATGA
78 L T I S S L Q P E D F A T Y Y C S O S T

361 CATGTCCCGC TCACGTTTGG ACAGGGTACC AAGGTGGAGA TCAAACGAAC TGTGGCTGCA
GTACAGGGCG AGTGCAAACC TGTCCCATGG TTCCACCTCT AGTTTGCTTG ACACCGACGT
98 H V P L T F G Q G T K V E I K R T V A A

421 CCATCTGTCT TCATCTTCCC GCCATCTGAT GAGCAGTTGA AATCTGGAAC TGCTTCTGTT
GGTAGACAGA AGTAGAAGGG CGGTAGACTA CTCGTCAACT TTAGACCTTG ACGAAGACAA
118 P S V F I F P P S D E Q L K S G T A S V

481 GTGTGCCTGC TGAATAACTT CTATCCAGA GAGGCCAAAG TACAGTGGA GGTGGATAAC
CACACGGACG ACTTATTGAA GATAGGGTCT CTCCGGTTTC ATGTCACCTT CCACCTATTG
138 V C L L N N F Y P R E A K V Q W K V D N

541 GCCCTCCAAT CGGGTAACTC CCAGGAGAGT GTCACAGAGC AGGACAGCAA GGACAGCACC
CGGGAGGTTA GCCCATTGAG GGTCTCTCA CAGTGTCTCG TCCTGTCGTT CCTGTCGTGG
158 A L Q S G N S Q E S V T E Q D S K D S T

601 TACAGCCTCA GCAGCACCTT GACGCTGAGC AAAGCAGACT ACGAGAAACA CAAAGTCTAC
ATGTCGGAGT CGTCGTGGGA CTGCGACTCG TTTCGTCTGA TGCTCTTTGT GTTTCAGATG
178 Y S L S S T L T L S K A D Y E K H K V Y

661 GCCTGCGAAG TCACCCATCA GGGCCTGAGC TCGCCCGTCA CAAAGAGCTT CAACAGGGGA
CGGACGCTTC AGTGGGTAGT CCCGACTCG AGCGGGCAGT GTTCTCTGAA GTTGTCCCCT
198 A C E V T H Q G L S S P V T K S F N R G

721 GAGTGTTAAG CTGATCCTCT ACGCCGGACG CATCGTGGCC CTAGTACGCA ACTAGTCGTA
CTCACAATTC GACTAGGAGA TCGGCCCTGC GTAGCACC GG GATCATGCGT TGATCAGCAT
218 E C O

FIG. 36



781 AAAAGGGTAT CTAGAGGTTG AGGTGATTTT ATGAAAAAGA ATATCGCATT TCTTCTTGCA
TTTTCCCATA GATCTCCAAC TCCACTAAAA TACTTTTCT TATAGCGTAA AGAAGAACGT
-1 M K K N I A F L L A

841 TCTATGTTTCG TTTTCTCTAT TGCTACAAAC GCGTACGCTG AGGTTTCAGCT AGTGCAGTCT
AGATACAAGC AAAAAAGATA ACGATGTTTG CGCATGCGAC TCCAAGTCGA TCACGTCAGA
-11 S M F V F S I A T N A Y A E V Q L V Q S

901 GCGGGTGGCC TGGTGCAGCC AGGGGGCTCA CTCCGTTTGT CCTGTGCAGC TTCTGGCTAC
CCGCCACCGG ACCACGTCGG TCCCCCGAGT GAGGCAAACA GGACACGTCG AAGACCGATG
8 G G G L V Q P G G S L R L S C A A S G Y

961 TCCTTCTCGA GTCACTATAT GCACTGGGTC CGTCAGGCCC CGGGTAAGGG CCTGGAATGG
AGGAAGAGCT CAGTGATATA CGTGACCCAG GCAGTCCGGG GCCCATTCCC GGACCTTACC
28 S F S S H Y M H W V R Q A P G K G L E W

1021 GTTGGATATA TTGATCCTTC CAATGGTGAA ACTACGTATA ATCAAAAGTT CAAGGGCCGT
CAACCTATAT AACTAGGAAG GTTACCACTT TGATGCATAT TAGTTTTCAA GTTCCCGGCA
48 V G Y I D P S N G E T T Y N O K F K G R

1081 TTCACTTTAT CTCGCGACAA CTCCAAAAAC ACAGCATACC TGCAGATGAA CAGCCTGCGT
AAGTGAAATA GAGCGCTGTT GAGGTTTTTG TGTCGTATGG ACGTCTACTT GTCGGACGCA
68 F T L S R D N S K N T A Y L Q M N S L R

1141 GCTGAGGACA CTGCCGTCTA TTACTGTGCA AGAGGGGATT ATCGCTACAA TGGTGA CTGG
CGACTCCTGT GACGGCAGAT AATGACACGT TCTCCCCTAA TAGCGATGTT ACCACTGACC
88 A E D T A V Y Y C A R G D Y R Y N G D W

1201 TTCTTCGACG TCTGGGGTCA AGGAACCCTG GTCACCGTCT CCTCGGCCTC CACCAAGGGC
AAGAAGCTGC AGACCCAGT TCCTTGGGAC CAGTGGCAGA GGAGCCGGAG GTGGTTCCCG
108 F F D V W G Q G T L V T V S S A S T K G

1261 CCATCGGTCT TCCCCCTGGC ACCCTCCTCC AAGAGCACCT CTGGGGGCAC AGCGGCCCTG
GGTAGCCAGA AGGGGGACCG TGGGAGGAGG TTCTCGTGGA GACCCCGTG TCGCCGGGAC
128 P S V F P L A P S S K S T S G G T A A L

1321 GGCTGCCTGG TCAAGGACTA CTTCCCCGAA CCGGTGACGG TGTCGTGGAA CTCAGGCGCC
CCGACGGACC AGTTCCTGAT GAAGGGGCTT GGCCACTGCC ACAGCACCTT GAGTCCGCGG
148 G C L V K D Y F P E P V T V S W N S G A

1381 CTGACCAGCG GCGTGCACAC CTTCCCGGCT GTCCTACAGT CCTCAGGACT CTACTCCCTC
GACTGGTTCG CGCACGTGTG GAAGGGCCGA CAGGATGTCA GGAGTCCTGA GATGAGGGAG
168 L T S G V H T F P A V L Q S S G L Y S L

1441 AGCAGCGTGG TGACCGTGCC CTCCAGCAGC TTGGGCACCC AGACCTACAT CTGCAACGTG
TCGTGCGACC ACTGGCACGG GAGGTCGTG AACCCGTGGG TCTGGATGTA GACGTTGCAC
188 S S V V T V P S S S L G T Q T Y I C N V

1501 AATCACAAGC CCAGCAACAC CAAGGTGCAG AAGAAAGTTG AGCCCAAATC TTGTGACAAA
TTAGTGTTTCG GGTCGTTGTG GTTCCAGCTG TTCTTTCAAC TCGGGTTTAG AACACTGTTT
208 N H K P S N T K V D K K V E P K S C D K

1561 ACTCACACAT GCGCGCCGTG CCCAGCACCA GAACTGCTGG GCGGCCGCAT GAAACAGCTA
TGAGTGTTGTA CGGGCGGCAC GGGTCGTGGT CTTGACGACC CGCCGGCGTA CTTTGTGAT
228 T H T C P P C P A P E L L G G R M K Q L

FIG. 37A



1621 GAGGACAAGG TCGAAGAGCT ACTCTCCAAG AACTACCACC TAGAGAATGA AGTGGCAAGA
CTCCTGTTCC AGCTTCTCGA TGAGAGGTTC TTGATGGTGG ATCTCTTACT TCACCGTTCT
248 E D K V E E L L S K N Y H L E N E V A R

1681 CTCAAAAAGC TTGTCGGGGA GCGCTAA
GAGTTTTTCG AACAGCCCCT CGCGATT
268 L K K L V G E R O

FIG. 37B

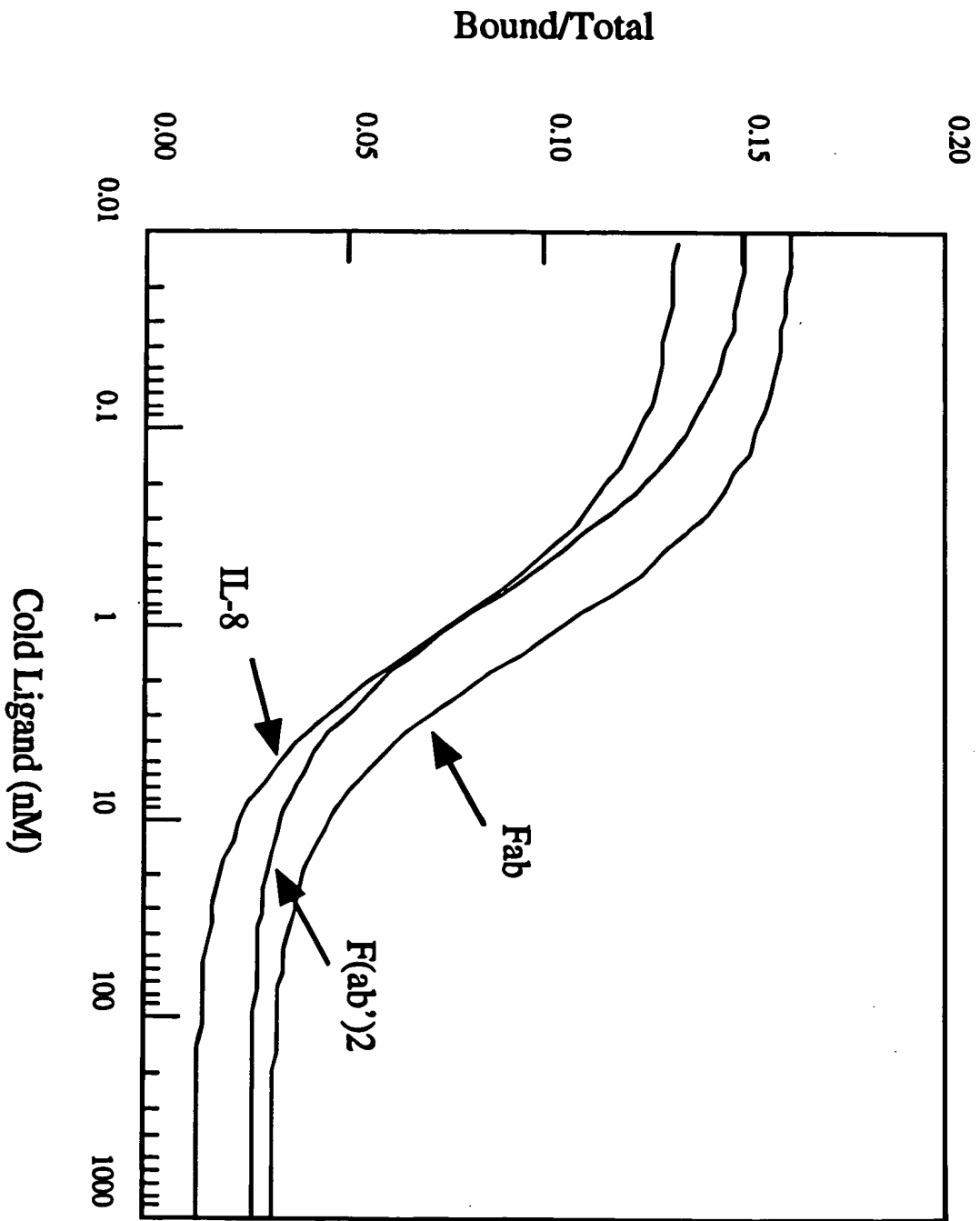


FIG. 38

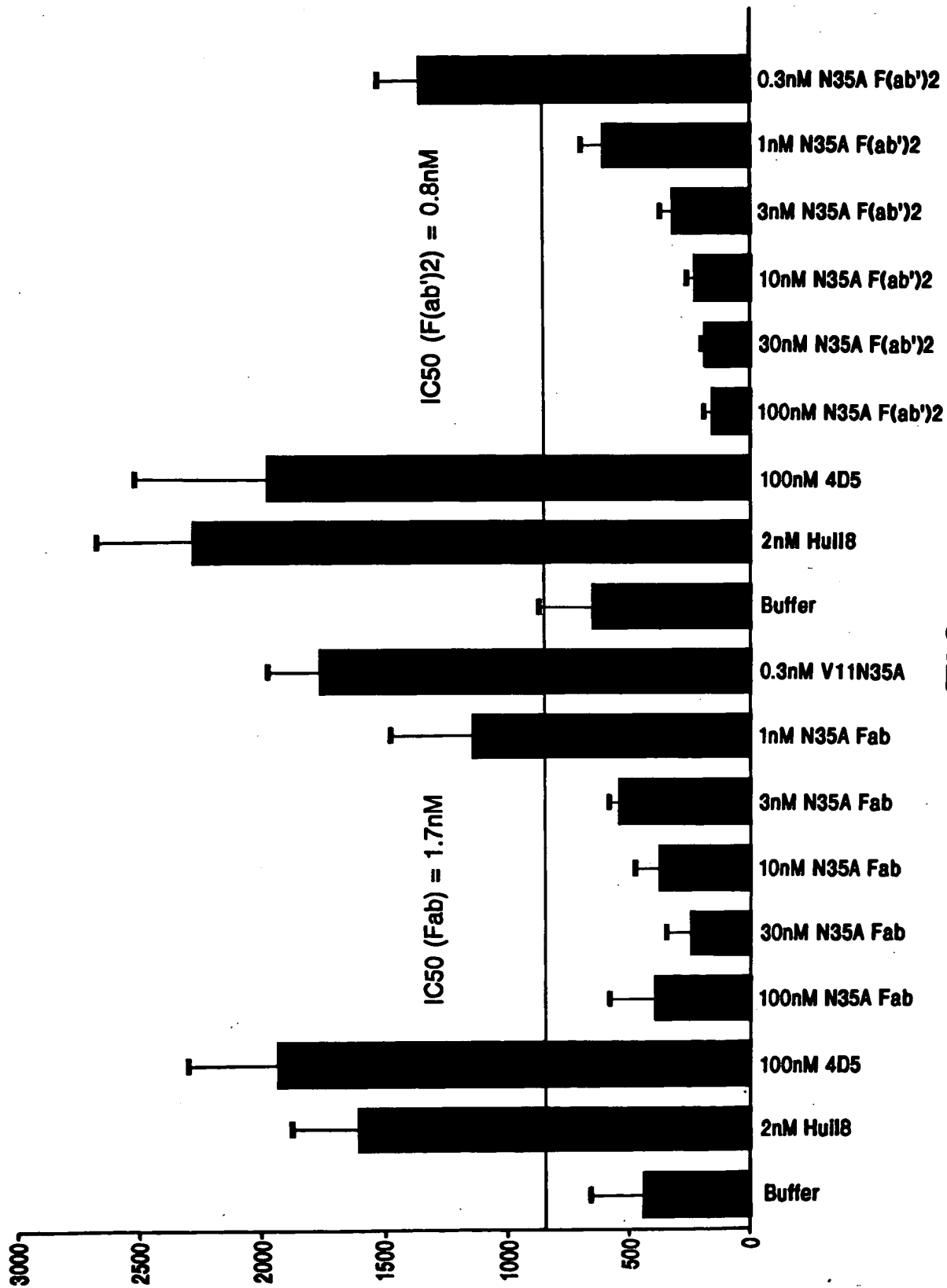


FIG. 39

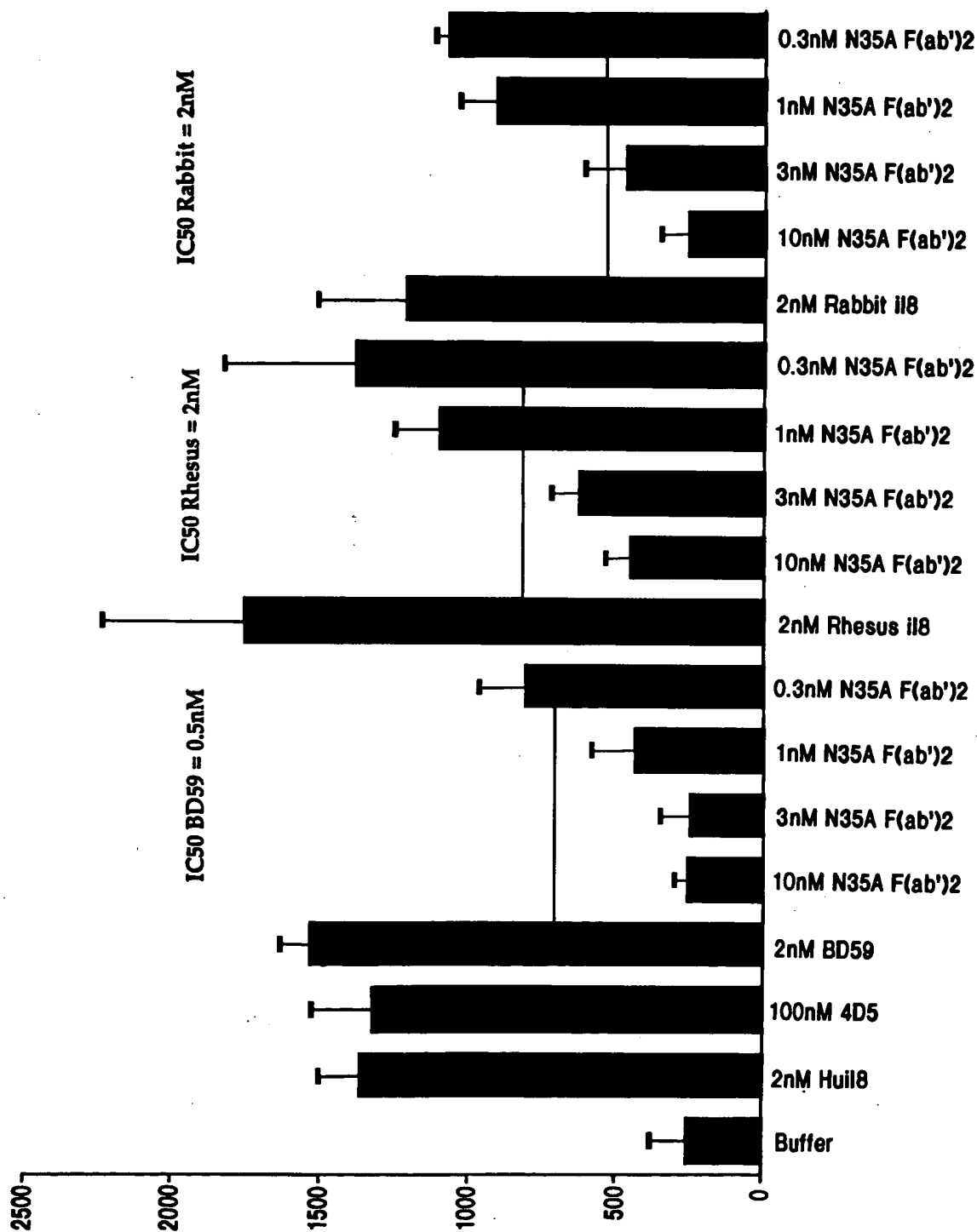


FIG. 40



ecoRI pflMI pleI
apoI bslI mboII taqI
1 GAATTCAACT TCTCCATACT TTGGATAAGG AAATACAGAC ATGAAAATC TCATTGCTGA GTTGTATTTT AAGCTTGCCC AAAAAGAGA AGAGTCGAAT
CTTAAGTTGA AGAGGTATGA AACCTATTCC TTATGTCGTG TACTTTTAG AGTAAGGACT CAACAATAA TTCGAACGGG TTTTCTCTCT TCTCAGCTTA
bepMI
hinPI hhal/cfoI mboII/ndeII[dam-]
mstI avII/fspI hindIII dpnI[dam+]
101 GAACTGTGTG CGCAGGTAGA AGCTTTGGAG ATTATCGTCA CTGCAATGCT TCGCAATATG GCGCAAAATG ACCAACAGCG GTTGATTGAT CAGGTAGAGG
CTTGACACAC GCGTCCATCT TCGAACCTC TAATAGGACT GAGGTACGA AGCGTTATAC CGGTTTTTAC TGGTTGTGCG CAACTAATA GTCCATCTCC
rsal
hinPI hhal/cfoI mnlI
haeII csp6I sfanI bsmI
201 GGGCGCTGA CGAGGTAAAG CCGGATGCCA GCATTCCCTGA CGACGATACG GAGCTGCTGC CGGATTACGT AAAGAAGTTA TTGAAGCATC CTCGTCACTA
CCGCGGACAT GTTCCATTTC GGGCTACGGT CGTAAGGACT GCTGCTATGC CTCGACGACG CGCTAATGCA TTTCTTCAAT AACCTCGTAG GAGCAGTCAT
thaI
fnuDII/mvnl
fnu4HI
bsoFI
bbvI maeII
fnu4HI bstvI snaBI
bsoFI bsh1236I
bbvI hinPI bsaAI
aluI hhal/cfoI
301 AAAAGTTAAT CTTTCAACA GCTGTCAATA AGTTGTCAAG AGTTGTCAAG CCGGACTT ATAGTCGCTT TGTCTTTTAT TTTTAACTA TTTGTAATA GAATTCGAGC
TTTCAATTA GAAAGTTGT CGACAGTATT TCACAGCTGC CCGCTCTGAA TATCAGCGAA ACAAAATAA AAATATCAT AAACATGAT CTTAAGCTCG
haeIII/palI
mcrI
eagI/xmaII/ecI XI
eaeI
cfrI
bsiEI ahdII/eam1105I
maeIII bsmAI
tru9I aluI
mseI pvuII
nspBII
tru9I mseI
maeIII apoI banII
bfaI taqI
maeI bmyI
rmaI
ecoRI bsp1286
bsiHKA I
hgiJII
hgiAI/aspBI
ecI136II

FIG. 41A



```
scrFI
ncII
mspI
hpaII
dsav
xmaI/pspAI
smaI
scrFI
ncII
dsav
cauII
bsaJI
    xhoI
    mnlI
    avai
        sau3AI taqI
        mboI/ndeII[dam-]
        cep6I
        nlaIV nlaIV paer7I
        kpni cauII dpuII[dam-]
        hgici bstYI/xhoII
        bani bsaJI alwI[dam-]
        asp718 bamHI avai
        acc65I alwI[dam-] mnlI mnlI
        mboII sfaNI
501 TCGGTACCCG GGGATCCTCT CGAGGTGAG GTGATTTTAT GAAAAGAAT ATCGCATTTT TCTTGCAATC TATGTTCCGT TTTTCTATTG CTACAAACGC
    AGCCATGGGC CCTAGGAGA GTCCAACTC CACTAAATA CTTTTCTTA TAGCGTAAG AGAACGCTAG ATACAAGCAA AAGAGATAAC GATGTTGCG
    M K K N I A F L L A S M F V F S I A T N A
-23 a mutation was found that inactivated the mluI site. The penultimate nucleotide was changed fr G toT ^

sstI
sacI
hgIIII
hgIAI/aspEI
ecl136II
bsp1286
bsiHKAI
    bsmFI bmyI
        bsrI avai aluI
            mnlI
            acII
            tth111I/aspI banII
            ecoRV
501 ATACGCTGAT ATCCAGATGA CCCAGTCCC CGAGTCCCCTG TCCGCCTCTG TGGCGATAG GGTCACTATC ACCTGCAGCT CAAGTCAAG CTAGTACAT
    TATGCCACTA TAGGTCTACT GGTGAGGGG CTGAGGGGAG AGCGGGAGAC ACCCGTATC CCAGTGTAG TGGACGTCCA GTTCAGTTTC GAATCATGA
-2 Y A D I Q M T Q S P S S L S A S V G D R V T I T C R S S Q S L V H
```

FIG. 41B

scrFI
 mvaI
 ecorII
 dsav
 bstNI
 bsrI
 apyI[dam+]

601 GGTATAGGTG CTACGTATTTT CAACAGAAAC CAGGAAAGC TCCGAACTA CTGATTACA AAGTATCCAA TCGATTCTCT GGAGTCCCTT
 CCATATCCAC GATGCATAAA TGTGACCATTA GTTGTCTTTC GTCTTTTCG AGGCTTTGAT GACTAAATGT TCCATAGGTT AGCTAAGAGA CCTCAGGGAA
 32 G I G A T Y L H W Y Q Q K P G K A P K L L I Y K V S N R F S G V P S

mapi
 hpaiI
 bali
 bsawI
 sau3AI
 mboI/ndeII[dam-]
 dpnI[dam+]
 dpnII[dam-]
 alwI[dam-]
 nlaIV
 bstYI/xhoII
 bamHI
 alwI[dam-] bsmFI
 alwI[dam-] TCGATCCGGT TCTGGGACGG ATTTCATCTT GACCATCAGC AGTCTGCAGC CAGAGACTT CGCACTTAT TACTGTTTAC AGAGTACTCA
 701 GAGCGAAGAG ACCTAGGCCA AGACCTGCC TAAAGTGAGA CTGTAGTTCG TCAGACGTCG GTCCTCTGAA GCCTTGAATA ATGACAAGTG TCTCATGAGT
 66 R F S G S G S G T D F T L T I S S L Q P E D F A T Y X C S Q S T H

styI
 bsajI
 rsal
 csp6I
 nlaIV
 kpnI
 hgiCI
 bani
 asp718
 maeII
 acc65I
 ber8I
 aciI
 bamFI

sau3AI
 mboI/ndeII[dam-]
 dpnI[dam+]
 dpnII[dam-]
 fnu4HI
 bsoFI
 bbvI
 mboII
 bpuAI
 bbsI
 aciI
 mboII

801 TGTCCGCTC ACGTTTGGAC AGGTGACCAA GGTGGAGATC AAACAACTG TGGCTGCACC ATCTGCTTC ATCTCCGC CATCTGATGA GCAGTTGAAA
 ACAGGGCCAG TGCAAACCTG TCCCATGGTT CCACCTCTAG TTTCCTTAG ACCGACGTGG TAGACAGAAG TAGAAGGGCG GTAGACTACT CGTCAACTTT
 99 V P L T F G Q G T K V E I K R T V A A P S V F I F P P S D E Q L K

tfiI
 hinfi
 taqI
 clai/bsp106
 bspDI[dam-]
 hinfi

601 GGTATAGGTG CTACGTATTTT CAACAGAAAC CAGGAAAGC TCCGAACTA CTGATTACA AAGTATCCAA TCGATTCTCT GGAGTCCCTT
 CCATATCCAC GATGCATAAA TGTGACCATTA GTTGTCTTTC GTCTTTTCG AGGCTTTGAT GACTAAATGT TCCATAGGTT AGCTAAGAGA CCTCAGGGAA
 32 G I G A T Y L H W Y Q Q K P G K A P K L L I Y K V S N R F S G V P S

mapi
 hpaiI
 bali
 bsawI
 sau3AI
 mboI/ndeII[dam-]
 dpnI[dam+]
 dpnII[dam-]
 alwI[dam-]
 nlaIV
 bstYI/xhoII
 bamHI
 alwI[dam-] bsmFI
 alwI[dam-] TCGATCCGGT TCTGGGACGG ATTTCATCTT GACCATCAGC AGTCTGCAGC CAGAGACTT CGCACTTAT TACTGTTTAC AGAGTACTCA
 701 GAGCGAAGAG ACCTAGGCCA AGACCTGCC TAAAGTGAGA CTGTAGTTCG TCAGACGTCG GTCCTCTGAA GCCTTGAATA ATGACAAGTG TCTCATGAGT
 66 R F S G S G S G T D F T L T I S S L Q P E D F A T Y X C S Q S T H

styI
 bsajI
 rsal
 csp6I
 nlaIV
 kpnI
 hgiCI
 bani
 asp718
 maeII
 acc65I
 ber8I
 aciI
 bamFI

sau3AI
 mboI/ndeII[dam-]
 dpnI[dam+]
 dpnII[dam-]
 fnu4HI
 bsoFI
 bbvI
 mboII
 bpuAI
 bbsI
 aciI
 mboII

801 TGTCCGCTC ACGTTTGGAC AGGTGACCAA GGTGGAGATC AAACAACTG TGGCTGCACC ATCTGCTTC ATCTCCGC CATCTGATGA GCAGTTGAAA
 ACAGGGCCAG TGCAAACCTG TCCCATGGTT CCACCTCTAG TTTCCTTAG ACCGACGTGG TAGACAGAAG TAGAAGGGCG GTAGACTACT CGTCAACTTT
 99 V P L T F G Q G T K V E I K R T V A A P S V F I F P P S D E Q L K

tfiI
 hinfi
 taqI
 clai/bsp106
 bspDI[dam-]
 hinfi

FIG. 41C

cac8I
aluI
sstI
sacI
hgIuII
hgIAI/aspHI
ecII36II
bsp1286
bsIHKAI
bmyI
haeIII/pali
sau96I banII
asuI ddei
hphI
ecoOI09I/draII
maeIII alwNI[dcn-]
1101 CTGGGAAGTC ACCCATCAGG GCCTGAGCTC GCCCGTCACA AAGAGCTTCA ACAGGGGAGA GTGTTAGCT GATCCTCTAC GCCGGACGCA TCGTGGCCCT
GACGCTTCAG TGGGTAGTCC CGGACTCGAG CCGGCACTGT TTCTCGAAGT TGTCCCTCT CACAAATCGA CTAGGAGATG CGGCCTGCCT AGCACCGGGA
199 C E V T H Q G L S S P V T K S F N R G E C O

FIG. 41D



1201 AGTACGCAAC TAGTCGTAAA AAGGTTATCT AGAGGTTGAG GTGATTTTAT GAAAGAAGAT ATCGCATTC TTCTTGCAATC TATGTTGCTT TTTTCTATTG
TCATGCGTTG ATCAGCATTT TTCCCATAGA TCTCCAATC CACTAAATA CTTTTCTTA TAGCGTAAAG AAGAACGTAG ATACAAGCAA AAAAGATAAC
M K K N I A P L L A S M F V F S I A

-23

1301 CTACAAAGC GTACGCTGAG GTTCAGCTAG TGCAGTCTG CGGTGGCTG GTGCAGCCAG GGGCTCACT CCGTTTGTC TGTGCAGCTT CTGGCTACTC
GATGTTGCG CATCGACTC CAGTCGATC ACGTGACAC GCCACCGAC CCGGCTGTC CCGGAGTGA GGCAACAGG ACACGTGCGA GACCGATGAG
-5 T N A Y A E V Q L V Q S G G L V Q P G G S L R L S C A A S G Y S

FIG. 41E

FIG. 41F

nlaIV
 hgiCI
 bani
 scrFI
 mvaI
 ecorII
 dsav
 bstNI
 sau96I dsav
 haeIII/pali bstNI
 fnu4HI
 bsoFI bsajI bslI
 acilI apyI[dcmt+]
 bsp1286 asuI bsoFI
 bmyI nsplII bsajI bbyI apyI[dcmt+] bslI ageI maelIII
 cfr10I/bsrFI
 bsawI tthl11I/aspl
 bsalI ageI maelIII
 TCCCGAACC GGTGACGGTG
 TTCCTGATGA AGGGGCTTGG CCACTGCCAC
 P L A P S S K S T S G G T A A L G C L V K D Y F P E P V T V
 hinPI
 hbai/cfoI
 nlaIV
 nari
 kasi
 hinII/acylI
 hgiCI
 haell
 bani
 ddei abail/bsahi nsplII alw44I/snoi cauli
 scfi bsu36I/mstII/sauI mnlI bbvI bsteII bmyI bpmI/gsuI[dcmt-]
 accacCTTGA GTCCGGGGGA CTGGTCGCCG CACTGTGGA AGGGCCGACA GGATGTCAGG AGTCCTGAGA TGAGGGAGTC GTCCGACCAC TGCACGGGA
 162 S W N S G A L T S G V H T F P A V L Q S S S G L Y S L S S V V T V P S
 aluI nlaIV
 fnu4HI
 bsoFI
 bbvI
 bstXI
 ccagcagCTT GGGCACCAG ACCTACATCT GCACGTGAA TCACAGCCC AGCACACCA AGGTGACAA GMAAGTTGAG CCCAAATCTT GTGACAAAAC
 GGTGTCGAA CCGTGGCTC TGGANGTAGA CGTGCACCTT AGTGTCGGC AGTGTTCGGG TCGTGTGGT TCCAGCTGTT CTTTCAACTC GGGTTAGAA CACTGTGTTG
 196 S S L G T O T Y I C N V N H K P S N T K V D K K V E P K S C D K T
 taqI
 sali
 styI hincII/hindII
 bsajI accI
 banII
 maelII
 hgiJII
 bsp1286
 bmyI
 hgiJII
 bsp1286
 bmyI
 banII
 maelII

FIG. 41G

[illegible]

FIG. 41H



2301 AATGCGCTCA TCGTCATCCT CGGCACCGTC ACCCTGGATG CTGTAGGCAT AGGCTTGGTT ATGCCGGTAC TGCCGGGCTT CTTGCGGGAT ATCGTCCATT
TTACGGGAGT AGCAGTAGGA GCGGTGGCAG TGGGACCTAC GACATCCGTA TCCGAACCAA TACGGCCATG ACGGCCCGGA GAACGCCCTA TAGCAGGTAA

2401 CCGACAGCAT CGCCAGTCAC TATGGCGTGC TGCTAGCGCT ATATGCGTTC ATGCAATTTC TATGCCGACC CGTTCTCGGA GCACTGTCCG ACGGCTTTGG
GGCTGTGCTA GCGGTCACTG ATACCGCAGC ACGATCGCGA TATACGCNAC TACGTTAAG ATACGGCTGG GCAAGAGCCT CGTGACAGGC TGCGGNAACC

2501 CGCGCGCCCA GTCTGTCTCG CTTGCTACT TGGAGCCACT ATCGACTACG CGATCATGCG GACACACCC GTCTGTGGA TCCTCTACGC CGGACGCATC
GGCGGGGGT CAGGACGAGC GAAGCGATGA ACCTGGGTGA TAGCTGATGC GCTAGTACCG CTGCTGTGGG CAGGACACCT AGGAGATCGG GCCTGCGTAG

FIG. 41I

FIG. 41J



2901 TGGGCGGG GCATGACTAT CGTCGCCGCA CTTATGACTG TCYTCTTTAT CATGCAACTC GTAGGACAGG TGCCGGCAGC GCTCTGGGTC ATTTTCGGCG
ACCGCGCCC CGTACTGATA GCAGCGGGGT GAATGACTGAC AGAAGAATA GTACGTTGAG CATCCTGTCC ACGCGCGTCG CGAGACCCAG TAAAGCCGCG

3001 AGGACCGCTT TCGCTGGAGC GCGACGATGA TCGGCCGTGTC CTTTCGGGTA TTGGGAATCT TGCACGCCCT CGCTCAAGCC TTCTCACTG GTCCCGCCAC
TCCTGGCGAA AGGACCTCG CGCTGCTACT AGCGGACAG CGAACCCAT AACCTTAGA ACGTGGGGA ACGTGGGGA CGGAGTTGG AGCAGTGAC CAGGCGGTG

3101 CAAACGTTTC GCGGAGAGC AGGCCATTAT CGCGGCATG CGCGCGACG CGCTGGGCTA CGTCTTGTG CGCTTGGGA CGGAGGCTG GATGCGCTTC
GTTGCAAG CGCTCTTCG TCCGGTAATA GCGCGCTAC CGCGGCTGC GCGACCGAT GCAGAACGAC CGCAGCGCT GCGCTCGAC CTACCGGAG

2901 TGGGCGGG GCATGACTAT CGTCGCCGCA CTTATGACTG TCYTCTTTAT CATGCAACTC GTAGGACAGG TGCCGGCAGC GCTCTGGGTC ATTTTCGGCG
ACCGCGCCC CGTACTGATA GCAGCGGGGT GAATGACTGAC AGAAGAATA GTACGTTGAG CATCCTGTCC ACGCGCGTCG CGAGACCCAG TAAAGCCGCG

3001 AGGACCGCTT TCGCTGGAGC GCGACGATGA TCGGCCGTGTC CTTTCGGGTA TTGGGAATCT TGCACGCCCT CGCTCAAGCC TTCTCACTG GTCCCGCCAC
TCCTGGCGAA AGGACCTCG CGCTGCTACT AGCGGACAG CGAACCCAT AACCTTAGA ACGTGGGGA ACGTGGGGA CGGAGTTGG AGCAGTGAC CAGGCGGTG

3101 CAAACGTTTC GCGGAGAGC AGGCCATTAT CGCGGCATG CGCGCGACG CGCTGGGCTA CGTCTTGTG CGCTTGGGA CGGAGGCTG GATGCGCTTC
GTTGCAAG CGCTCTTCG TCCGGTAATA GCGCGCTAC CGCGGCTGC GCGACCGAT GCAGAACGAC CGCAGCGCT GCGCTCGAC CTACCGGAG

FIG. 41K



3201 CCCATTATGA TTCTTCTCGC TTCGGCGGC ATCGGGATGC CCGCGTTGCA GGCCATGCTG TCCAGGCAGG TAGATGACGA CCATCAGGGA CAGCTTCAAG
GGGTAATACT NAGAAGAGCG NAGGCGCGCG TAGCCCTACG GCGCGAACGT CCGGTACGAC AGGTCCGTCC ATCTACTGCT GTCGAAGTTC

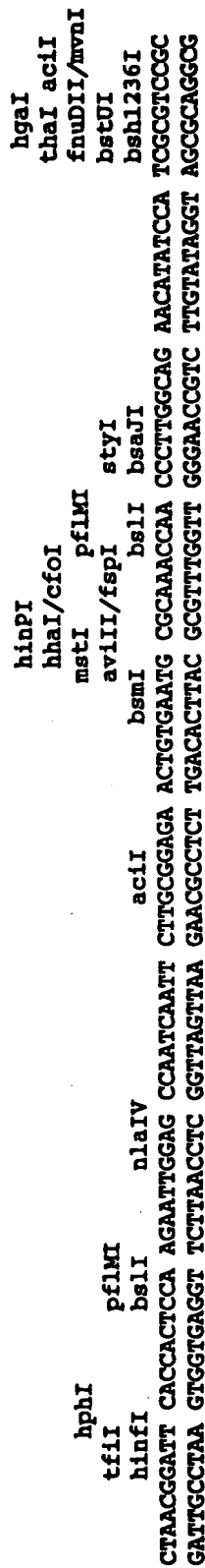
```

fnu4HI
bsoFI
aciI
thai
fnuDI1/mvni
bstUI
cac8I
sau3AI bsh1236I
mboI/ndeII[dam-]
dpnI[dam+]
dpnII[dam-]
dpnII[dam+]
taqI[dam-]
aciI dpnII[dam-]
ggcTCTTACC AGCCTAACTT CGATCACTGG ACCGCTGATC GTCACGGCGA TTTATGCCGC CTCGGCGAGC ACATGGAACG GGTTGGCATG
3301 GATOGCTCGC CCGAGAATGG TCGGATTGAA GCTAGTGACC TGGGACTAG CAGTCCCGCT AAATACGGCG GAGCGGCTCG TGTACCTTGC CCMACCGTAC

```

[illegible]

FIG. 41L



sau3AI
mboI/ndeII[dam-]
mami[dam-]
dpmI[dam+]
dpmII[dam-]
bstYI/xhoII
alwI[dam-]
mspI
hpaII
mroI bsaBI[dam-]
bspMI
bspEI[dam-]
bsaWI sfanI
accII[dam-] foki cac8I
fnu4HI
bsOFI
bbvI
sfanI
foki cac8I
33801 TGGTCTTCGG TTTCGGTGT TCGTAAAGTC TCGAAGCGG GAAGTCAGG CCTGCACCA TTATGTTCCG GATCTGCATC GCAGATGCT GCTGGCTACC
ACCAAGAGCC AAGGACAA AGCATTTTCG ACCTTTGGC CTTAGTGC GGGAGGTGGT AATACAAGC CTAGACGTAG CGTCTACGA CGACCGATGG
cac8I
foki
bsmFI
sau96I sfanI
nlaIV acII
avaII fnu4HI
asuI bsoFI
3901 CTGTGGNACA CCTACATCTG TATTACGAA GCGCTGGCAT TGACCTTGAG TGATTTTCT CTGGTCCCG CGCATCCATA CGCCAGTTG TTATCCCTCA
GACACCTTGT GGATGTAGAC ATATATGCTT CGGACCGTA ACTGGGACTC ACTAAAAGA GACCAGGGG CGTAGGTAT GCGGTCAAC AATGGGNGT
napi
scrFI
ncII
mspI
bsrI hpaII
bsII dsav nlaIII
maeII cauII
psp1406I maeIII nspHI
4001 CAACGTTCCA GTAACGGGC ATGTTCAATCA TCAGTAACCC GTATCGTGAG CATCTCTCT CGTTTCATCG GTATCATAC CCCCATGAC AGRAATTCCC
GTTCGAAGGT CATTTGCCCG TACAAGTAGT AGTCATTGGG CATAGCACTC GTAGGAGA GCAAGTAGC CATAGTAATG GGGGTACTTG TCTTTAAGGG
maeII
bsrI hpaII
bsII dsav nlaIII
maeII cauII
psp1406I maeIII nspHI
4001 CAACGTTCCA GTAACGGGC ATGTTCAATCA TCAGTAACCC GTATCGTGAG CATCTCTCT CGTTTCATCG GTATCATAC CCCCATGAC AGRAATTCCC
GTTCGAAGGT CATTTGCCCG TACAAGTAGT AGTCATTGGG CATAGCACTC GTAGGAGA GCAAGTAGC CATAGTAATG GGGGTACTTG TCTTTAAGGG

FIG. 41N

[illegible]

FIG. 410

hg1AI/aspHI
bsp1286
bsiHKAI
bmyI ndeI
apali/snoi
alw44I/snoi
delt
rsal
csp6I
GATTGTACTG AGAGTGCACC
CTAACATGAC TCTCAGGTGG

sfanI
fnu4HI
bsoFI
tru9I
bst1107I
bsri msel
acii
ACCGGAGTGT ATACTGGCTT AACATGCGG CATCAGAGCA GATTGTACTG AGAGTGCACC
TTGATACGCC CTAGTCTCGT

mbolI
earI/ksp632I
sapi
hinPI
hhal/cfoI
fnu4HI
pleI bsoFI mcrI
hinfi bbVI bsiEI
GCTCACTGAC TCGCTGCCGT CGGTCTTCG
AGCGAGGAG CGAGTGACTG AGCGACGGCA GCCAGCAAGC

bsII
cac8I
haeIII/pali
hael
nlaIII
nspl
nspHI
afIII
GGAAGAACA TGTGAGCAAA AGGCCAGCAA
CGATACGCT CCTTCTGT ACACCTGTT TCCGGTGGTT

hgaI
drdI
taqI
mfanI
GACGAGCATC ACAAATCG ACGCTCAAGT CAGAGTGC
CTGCTCGTAG TGTTTTAGC TCGAGTTCA GTCTCCACCG

fnu4HI
bsoFI
bbVI
maeII
maeIII
hinPI nlaIII bsri bsaAI
hhal/cfoI tth111I/aspI
acii
TGAAGGAGAA ATACCGCATC AGCGCTCTT CGCTTCCTC
TATCGGCTAG TCCGGAGAA GCGGAGGAG CGAGTGACTG AGCGACGGCA GCCAGCAAGC

acii
acii
sfanI
acii
acii
alul
acii
GCTGCGGCA GCGGTATCAG CTCACTCAA GCGGTATA CGGTATCCA CAGATCAG GGTATACGCA GGAAGAACA TGTGAGCAAA AGGCCAGCAA
CGACGCCGT CGCCATAGT CAGTGAGTTT CGGCCATAT GCCATAGT GTCTTAGTCC CCTATTGGT CCTTCTGT ACACCTGTT TCCGGTGGTT

fnu4HI
bsoFI
acii
fnu4HI
bsoFI
bsrBI
bbVI cac8I
alul
acii
GCTGCGGCA GCGGTATCAG CTCACTCAA GCGGTATA CGGTATCCA CAGATCAG GGTATACGCA GGAAGAACA TGTGAGCAAA AGGCCAGCAA
CGACGCCGT CGCCATAGT CAGTGAGTTT CGGCCATAT GCCATAGT GTCTTAGTCC CCTATTGGT CCTTCTGT ACACCTGTT TCCGGTGGTT

scrFI
mval
ecorII
dsav
bstNI
bsli
apyI[dcM+]
haeIII/pali
hael
nlaIV
fnuDII/mvnI
bstUI
bsh1236I
acii
fnu4HI
bsoFI
cac8I
haeIII/pali
hael
nlaIV
TCCATAGT CCGCCCCCT GACGAGCATC ACAAATCG ACGCTCAAGT CAGAGTGC
CGCGGGGGA CTGCTCGTAG TGTTTTAGC TCGAGTTCA GTCTCCACCG

4401 CGGGTGTGGG GCGCAGCCCA TGACCCAGTC ACGTAGCGAT AGCGAGTGT ATACTGGCTT AACATGCGG CATCAGAGCA GATTGTACTG AGAGTGCACC
GCCACAGCC CGCGGTGGT ACTGGGTCTG TGCATCGCTA TCGCCTCACA TATGACCGAA TTGATACGCC CTAGTCTCGT

4501 ATATCGGTG TGAATACCG CACAGATCGG TAAGGAGAAA ATACCGCATC AGCGCTCTT CGCTTCCTC GCTCACTGAC TCGCTGCCGT CGGTCTTCG
TATACGCCAC ACTTATGGC GTGTCTACGC ATTCTCTTT TATGGCTAG TCCGGAGAA GCGGAGGAG CGAGTGACTG AGCGACGGCA GCCAGCAAGC

4601 GCTGCGGCA GCGGTATCAG CTCACTCAA GCGGTATA CGGTATCCA CAGATCAG GGTATACGCA GGAAGAACA TGTGAGCAAA AGGCCAGCAA
CGACGCCGT CGCCATAGT CAGTGAGTTT CGGCCATAT GCCATAGT GTCTTAGTCC CCTATTGGT CCTTCTGT ACACCTGTT TCCGGTGGTT

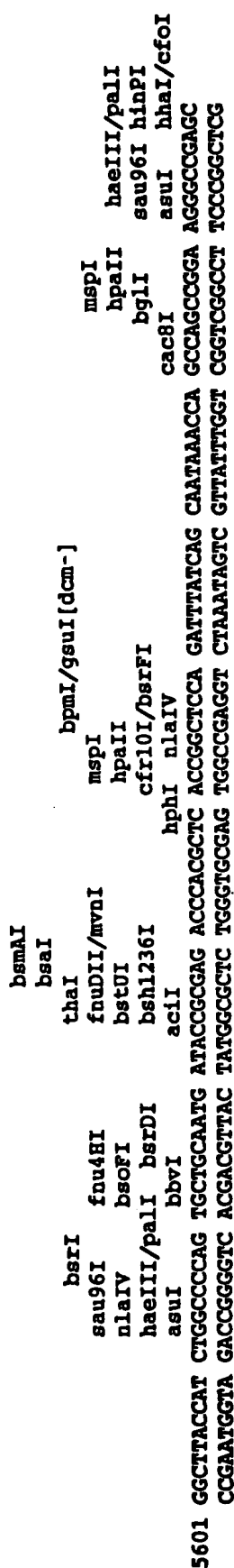
4701 AAGGCCAGGA ACCGTAAAAA GCGCGGTTG CTGGCGTTT TCCATAGT CCGCCCCCT GACGAGCATC ACAAATCG ACGCTCAAGT CAGAGTGC
TTCGGTCT TGGCATTTT COGGCCAC GACCGCAAA AGGTATCGA GCGCGGGGA CTGCTCGTAG TGTTTTAGC TCGAGTTCA GTCTCCACCG

FIG. 41P



[illegible]

FIG. 41R



mcrI
 bslEI
 bcgI
 fnu4HI
 bsoFI
 acII
 rsal
 bsrI
 scaI
 maeII hphI csp6I
 ddeI
 6001 ATTCTCTTAC TGTCAATGCA TCCGTAAGAT GCTTTTCTGT GACTGGTGAG TACTCAACCA AGTCATTCTG AGAATAGTGT ATGGGGGAC CGAGTTGCTC
 TAAGAGATG ACAGTACGGT AGGCATCTA CGAAAGACA CTGACCAC TCAGTTGCTG TCAAGTAAGAC TCATATCACA TAGCGCGCTG GCTCAACGAG
 bgaI
 hinII/acyI
 ahaII/bsaHI
 mspI
 hpaII
 scrFI
 nciI
 dsav
 cauII hincII/hindII
 aciI
 hinPI
 hhaI/cfoI
 thal
 fnuDII/mvnI
 bstUI
 bsh1236I
 hgiAI/aspHI
 bsp1286
 bsiHKAI
 bmyI
 apalI/snoI
 alw44I/snoI
 maeIII
 bssSI
 bstYI/xhoII
 alwiI/draI
 asp700 mboII
 6101 TTGCCCGCG TCAACACGGG ATAATACCG GCCACATAGC AGAATCTTAA AGTGTCTAT CATTTGGAAA CGTTCTTCGG GCGGAAAAC CTCAAGGATC
 AACGGGCGC AGTTGTGCCC TATTATGCGG CGGTGTATCG TCTTGAAAT TTCAAGAGTA GTAACTTTT GCAAGAGCC CCGCTTTTGA GAGTTCTCTAG
 bsrI
 sau3AI
 taqI
 mboI/ndeII[dam-]
 dpnI[dam+]
 dpnII[dam-]
 alwiI[dam-]
 bstYI/xhoII
 maeIII
 bssSI
 alw44I/snoI
 dpnI[dam+]
 dpnII[dam-]
 hgiAI/aspHI
 bsp1286
 bsiHKAI
 bmyI
 sau3AI
 sfanI
 mboI/ndeII[dam-]
 dpnI[dam+]
 dpnII[dam-]
 hphI
 6201 TTACCGCTGT TGAGATCCAG TTCGATGTAA CCCACTCGTG CACCAACTG ATCTTCAGCA TCTTTTACTT TCACCAGCGT TTCTGGGTGA GCAAAAACAC
 AATGGCGACA ACTCTAGTCT AAGCTACAT GGTGAGCAC GTGGGTGAC TAGAAGTCGT AGAAATGAA AGTGGTGGCA AAGACCCACT CGTTTTTCTC
 aciI
 fnu4HI
 bsoFI
 mboII
 earI/ksp632I
 sspI
 6301 GAAGGCNAA TGCGCNAAA AAGGGNATAA GGGCGACACG GAAATGTTGA ATACTCATC TCTTCTTTT TCAATATTAT TGAAGCATTT ATCAGGGTTA
 CTTCCGTTTT ACGGCGTTTT TTCCCTTAAT CCCTGTGTC CTTTACAACT TATGAGTATG AAGAGGAAA AGTTATAATA ACTTCGTAA TAGTCCCAAT

FIG. 41T



6401 TTGCTCTCATG ACCGATATCA TATTGAATG TATTAGAAA AATAACAAA TAGGGTTCC GGCACATTT CCGGAAAAG TCCACCTGA CGTCTAAGAA
AACAGAGTAC TCGCCTATGT ATAACTTAC ATAATCTTT TTATTGTTT ATCCCAAGG CGGTGTAAA GGGCTTTTC ACGTGGAAT GCAGATTCTT

6501 ACCATTATTA TCATGACATT AACCTATATA AATAGGCGTA TCACGAGGCC CTTTCGTCTT CAA
TGGTAATAAT AGTACTGTAA TTGGATATTT TTATCCGCAT AGTGCTCCG GAAGCAGAA GTT

Restriction enzymes and sites:

nlaiII rcaI bspHI acII bsmAI bsrBI
hinPI thal fndDII/mvnI bstUI bshI236I
maeII hinII/acyI shaII/bsaHI aatII ddeI
aciI nlaIV bhaI/cfoI
sau96I haeIII/palI asuI mboII
eco109I/draII mnlI bpuAI bbsI
nlaIII rcaI tru9I bspHI mseI
bssI

FIG. 41U



>length: 6563

aatII(GACGTC): 1645 6489
acc65I(GGTACC): 403 823
accI(GTMKAC): 1093 1963 4449
accII(TCCGGA): 3867[dam-]
acII(CCGC): 178 542 805 877 1340 1750 1826 2011 2039 2043 2182 2242 2384 2492 2501 2504
2628 2781 2784 2787 2906 2926 3005 3045 3094 3141 3226 3241 3309 3342 3367 3412
3436 3448 3490 3544 3597 3613 3619 3700 3838 3967 3970 3981 4139 4155 4210 4266
4351 4390 4400 4442 4467 4505 4518 4544 4561 4604 4611 4632 4723 4751 4878 4897
5018 5128 5263 5272 5634 5725 5916 5962 6083 6127 6204 6313 6412 6459
acyI see hinII
aflIII(ACRYGT): 1307 4678
ageI(ACCGT): 1788
ahaII/baaII(GRCGYC): 1645 1813 2616 2637 2751 3408 6107 6489
ahaII/draI(TTTAAA): 5435 5454 6146
ahdI/eam1105I(GACNNNNNGTC): 346 5566
aluI(AGCT): 72 121 252 320 398 532 589 648 1126 1144 1167 1325 1386 1906 2054 2075 2126
2218 2233 2889 3292 4202 4259 4270 4319 4338 4619 4845 4935 4981 5238 5759 5859
5922
alw44I/snoI(GTGCAC): 1831 4494 4992 6238
alwI[dam-](GGATC): 412 413 712 713 1171 1471 2578 2579 3300 3870 5245 5319 5331 5416 5429 5893
6196 6214
alwNI[dcm-](CAGNNNCTG): 1117 1385 5089
apaI(GGGCCC): 1695
apaLI/snoI(GTGCAC): 1831 4494 4992 6238
apoI(RAATY): 1 391 4093
apyI[dcm+](CCWGG): 640 999 1347 1357 1449 1665 1713 1755 1764 2333 3262 3645 4705 4826 4839
aseI/asnI/aspI(ATAAT): 5742
asnI see aseI
asp700(GAANNNTTC): 905 930 4234 6166
asp718(GGTACC): 403 823
asphi see hgiAI
aspi see thIIII
asuI(GGNCC): 1119 1195 1425 1434 1446 1512 1695 1696 1752 2155 2375 2727 3002 3090 3339 3463

FIG. 41V



Stop Template Primer

SL.97.2 5' CAT GGT ATA GGT TAA ACT TAT TTA CAC 3'

NNS Randomization Primer

SL.97.3 5' CAT GGT ATA GGT NNS ACT TAT TTA CAC 3'

FIG. 42



Randomization of Position N35 of Variable Light Chain CDR-1
Amino Acid Frequency

Phage Display (NNS Codon Library) Sort #3

Amino Acid	Frequency	% Total	IC50 (nM)
Asparagine (wt)	1	5.6	4.9
Glycine	6	16.6	3.1
Aspartic Acid	3	16.6	3.1
Glutamic Acid	4	22.2	0.1
Alanine	2	5.6	0.2
Lysine	1	5.6	ND
Serine	1	1.9	ND

FIG. 43A

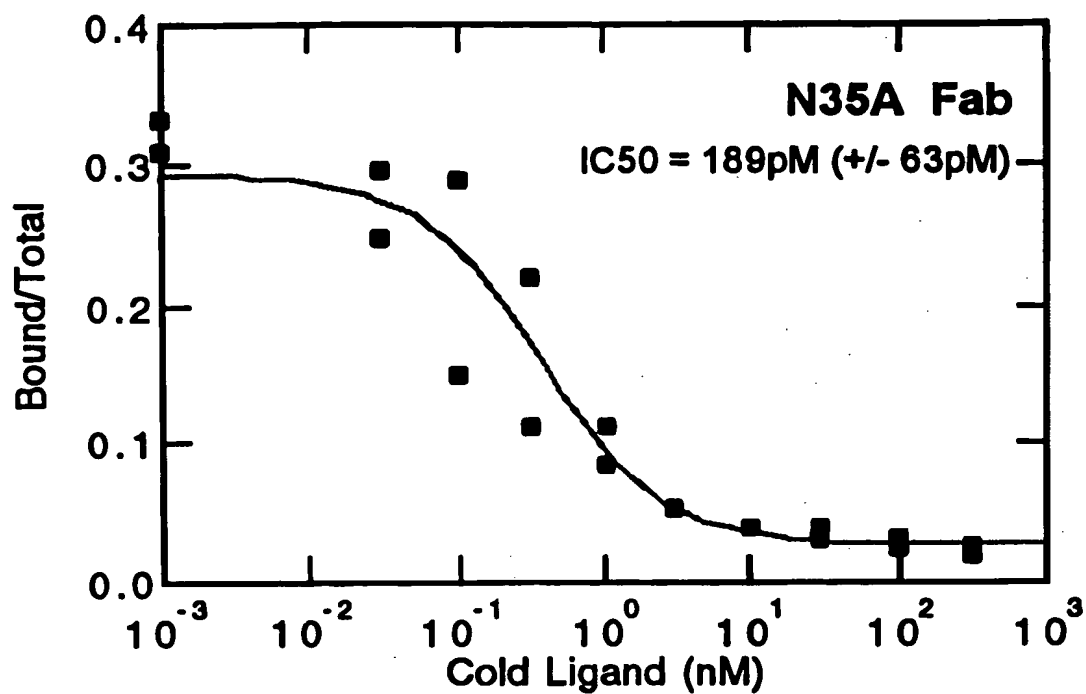


FIG. 43B-1

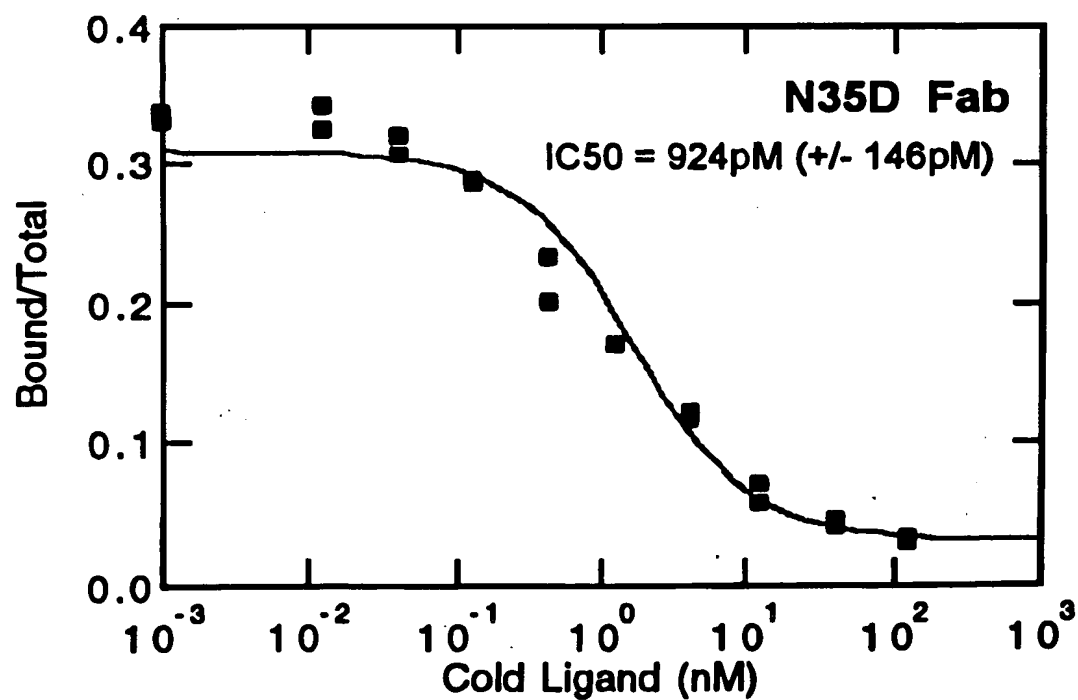


FIG. 43B-2

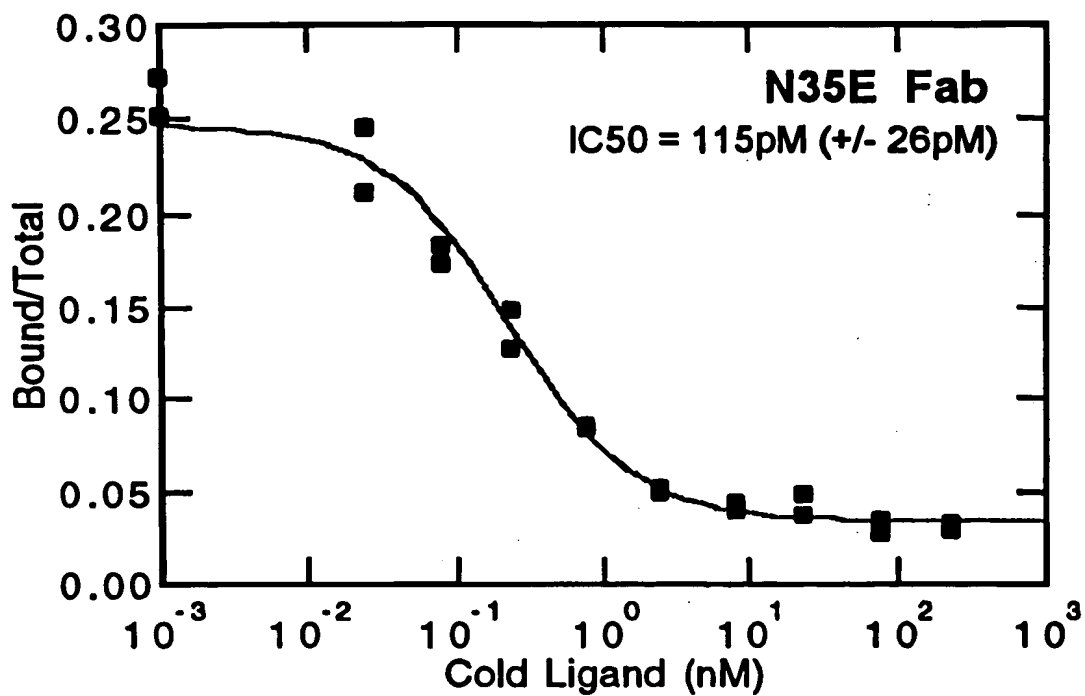


FIG. 43B-3

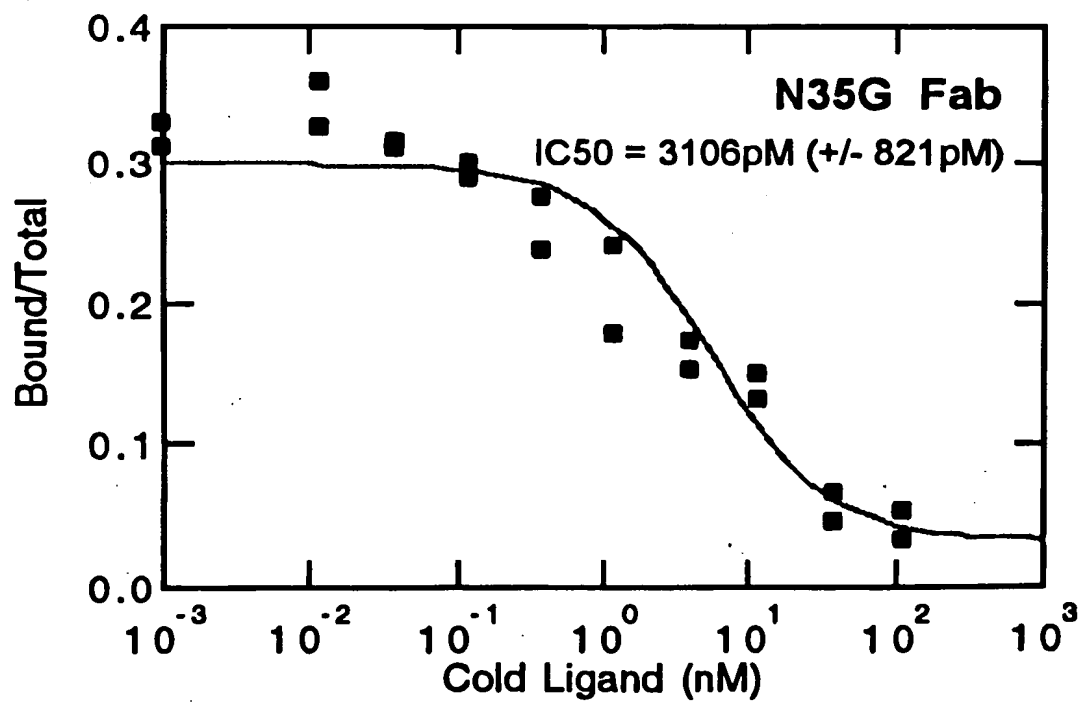
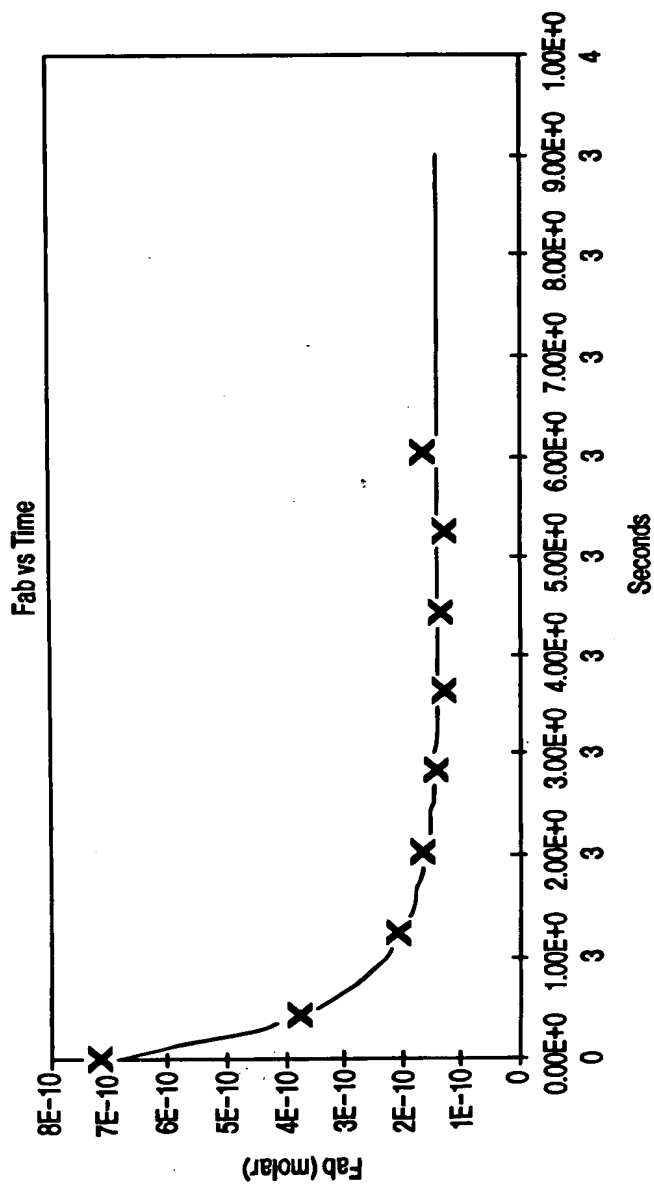


FIG. 43B-4



Representative Conc versus Time Plot. Shown is the kinetic data for 6G4V11N35A.F(ab')₂.

SAMPLE	ka	kd	Kd
6G4V11N35A-Fab	ND	ND	114pM
6G4V11N35A-F(ab') ₂	2.0x10 ⁶	2.1x10 ⁻⁴	109pM
6G4V11N35E-Fab	4.7x10 ⁶	2.6x10 ⁻⁴	54pM

FIG. 44



1 ATGAAAAAGA ATATCGCATT TCTTCTTGCA TCTATGTTTCG TTTTTCCTAT TGCTACAAAC
TACTTTTCT TATAGCGTAA AGAAGAACGT AGATACAAGC AAAAAAGATA ACGATGTTTG
-23 M K K N I A F L L A S M F V F S I A T N

61 GCATACGCTG ATATCCAGAT GACCCAGTCC CCGAGCTCCC TGTCCGCCTC TGTGGGCGAT
CGTATGCGAC TATAGGTCTA CTGGGTCAGG GGCTCGAGGG ACAGGCGGAG ACACCCGCTA
-3 A Y A D I Q M T Q S P S S L S A S V G D

121 AGGGTCACCA TCACCTGCAG GTCAAGTCAA AGCTTAGTAC ATGGTATAGG TGAGACGTAT
TCCAGTGGT AGTGGACGTC CAGTTCAGTT TCGAATCATG TACCATATCC ACTCTGCATA
18 R V T I T C R S S O S L V H G I G E T Y

181 TTACACTGGT ATCAACAGAA ACCAGGAAAA GCTCCGAAAC TACTGATTTA CAAAGTATCC
AATGTGACCA TAGTTGTCTT TGGTCCTTTT CGAGGCTTTG ATGACTAAAT GTTTCATAGG
38 L H W Y Q Q K P G K A P K L L I Y K V S

241 AATCGATTCT CTGGAGTCCC TTCTCGCTTC TCTGGATCCG GTTCTGGGAC GGATTTCACT
TTAGCTAAGA GACCTCAGGG AAGAGCGAAG AGACCTAGGC CAAGACCCTG CCTAAAGTGA
58 N R F S G V P S R F S G S G S G T D F T

301 CTGACCATCA GCAGTCTGCA GCCAGAAGAC TTCGCAACTT ATTACTGTTC ACAGAGTACT
GACTGGTAGT CGTCAGACGT CGGTCTTCTG AAGCGTTGAA TAATGACAAG TGTCTCATGA
78 L T I S S L Q P E D F A T Y Y C S O S T

361 CATGTCCCGC TCACGTTTGG ACAGGGTACC AAGGTGGAGA TCAAACGAAC TGTGGCTGCA
GTACAGGGCG AGTGCAAACC TGTCCCATGG TTCCACCTCT AGTTTGCTTG ACACCGACGT
98 H V P L T F G Q G T K V E I K R T V A A

421 CCATCTGTCT TCATCTTCCC GCCATCTGAT GAGCAGTTGA AATCTGGAAC TGCTTCTGTT
GGTAGACAGA AGTAGAAGGG CGGTAGACTA CTCGTCAACT TTAGACCTTG ACGAAGACAA
118 P S V F I F P P S D E Q L K S G T A S V

481 GTGTGCCTGC TGAATAACTT CTATCCAGA GAGGCCAAAG TACAGTGGAA GGTGGATAAC
CACACGGACG ACTTATTGAA GATAGGGTCT CTCCGGTTTC ATGTCACCTT CCACCTATTG
138 V C L L N N F Y P R E A K V Q W K V D N

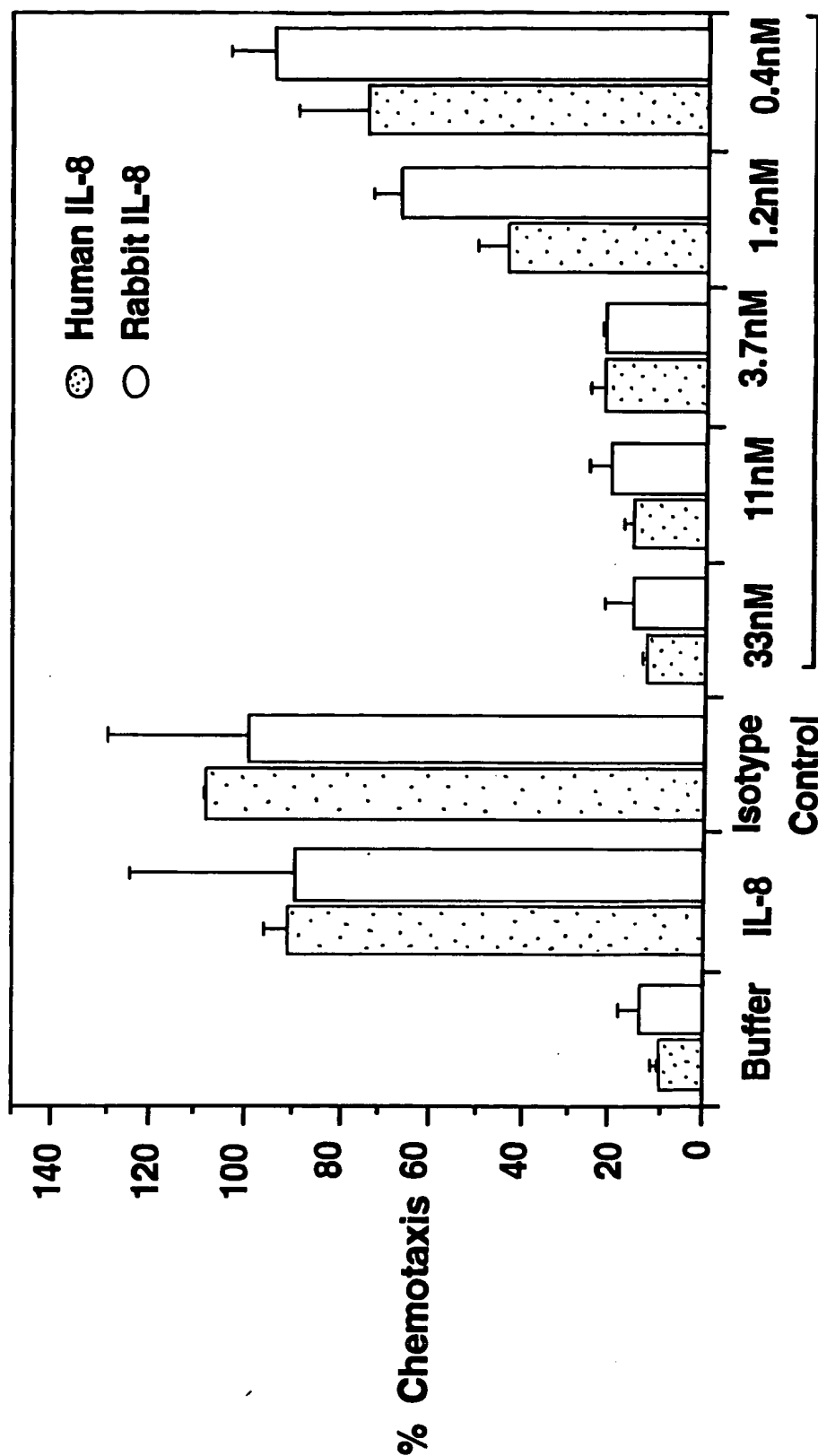
541 GCCCTCCAAT CGGGTAACTC CCAGGAGAGT GTCACAGAGC AGGACAGCAA GGACAGCACC
CGGGAGGTTA GCCCATTGAG GGTCTCTCA CAGTGTCTCG TCCTGTCGTT CCTGTCTGTTG
158 A L Q S G N S Q E S V T E Q D S K D S T

601 TACAGCCTCA GCAGCACCTC GACGCTGAGC AAAGCAGACT ACGAGAAACA CAAAGTCTAC
ATGTCGGAGT CGTCGTGGGA CTGCGACTCG TTTCGTCTGA TGCTCTTTGT GTTTCAGATG
178 Y S L S S T L T L S K A D Y E K H K V Y

661 GCCTGCGAAG TCACCCATCA GGGCCTGAGC TCGCCCGTCA CAAAGAGCTT CAACAGGGGA
CGGACGCTTC AGTGGGTAGT CCCGACTCG AGCGGGCAGT GTTCTCGAA GTTGTCCCCT
198 A C E V T H Q G L S S P V T K S F N R G

721 GAGTGTTAAG CTGATCCTCT ACGCCGGACG CATCGTGGCC CTAGTACGCA ACTAGTCGTA
CTCACAATTC GACTAGGAGA TCGGCCTGC GTAGCACC GG GATCATGCGT TGATCAGCAT
218 E C O

FIG. 45



Humanized Anti-IL-8

FIG. 46



N35AH1upr

5'-CTAGTGCAGTCTGGCGGTGGCCCTGGTGCAGCCAGGGGGCTCACTCCGTTTGTCTGTGCAGCTTCTGGCTACTCCTTC-3'

N35AH1lwr

5'-TCGAGAAGGAGTAGCCAGAAAGCTGCACAGGACAAACGGAGTGAGCCCCCTGGCTGCACCAGGCCACCCGCCAGACTGCAC
AG-3'

Bold indicates nucleotide change destroying PvuII site.

FIG. 47

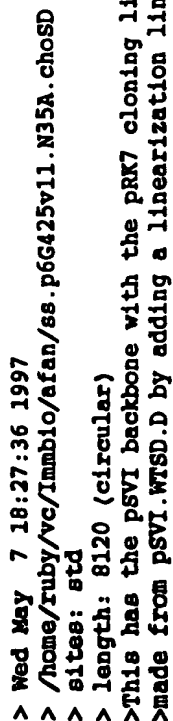


FIG. 48A



301 TATGCAGAGG CCGAGGCCGC CTGGCCCTCT GAGCTATTCC AGAAGTAGTG AGGAGCCTTT TTGGAGGCC TAGGCTTTTG CAAAAGCTA GCATTATCCG
ATACGCTCC GGCTCGGCG GAGCCGGAGA CTGGATAAGG TCTTCATCAC TCCTCGAA AACCTCGG ATCCGAAAC GTTTTCGAT CGAATAGGCC

301 TATGCAGAGG CCGAGGCCGC CTGGCCCTCT GAGCTATTCC AGAAGTAGTG AGGAGCCTTT TTGGAGGCC TAGGCTTTTG CAAAAGCTA GCATTATCCG
ATACGCTCC GGCTCGGCG GAGCCGGAGA CTGGATAAGG TCTTCATCAC TCCTCGAA AACCTCGG ATCCGAAAC GTTTTCGAT CGAATAGGCC

401 CCGGGAACGG TGCATTGGAA CGCGATTCC CGGTGCCAAG AGTGACGTAA GTACGCCCTA TAGAGCGATA AGAGGATTTT ATCCCGCTG CCATCATGTT
GGCCCTGCC ACCTAACCTT CGGCTAAGG GGCAGGTTT TCACTGCATT CATGCGGAT ATCTGCTAT TCTCTTAAA TAGGGGCGAC GGATAGTACCA
DHFR ATG*

501 TCGACCATTC AACTGCATCG TCGCCGTC CCAAAATATG GGGATTGGCA AGAAGGAGA CCTACCTGG CCTCCGCTCA GGAACGAGTT CAAGTACTTC
AGCTGCTAAC TTGACGTAGC AGCGGCACAG GCTTTTATAC CCTAACCGT TCTTGCCTCT GGATGGGACC GGAGGCGAGT CCTTGTCTCA GTTCATGAAG

FIG. 48B





hgaI
hinII/acyI
ahaII/baHI
scrFI
mvaI mnlI
ecorII
dsav
bstNI econI
apyI[dcmt+] mnlI
bsaJI bslI ddel
mnlI
901 GTGACGAGGA TCATGCAGGA ATTTCGAAGT GACACGTTTT TCCAGAAAT TGATTTGGGG AAATATAAAC CTCTCCAGC ATACCCAGGC GTCTCTCTG
CACTGTCTCT AGTACGTCTT TAACTTTCA CTGTGCAAAA AGGTCTTTA ACTAAACCC TTTATATTG GAGAGGTCT TATGGGTCCG CAGGAGAGAC

scrFI
mvaI
ecorII
dsav
bstNI
apyI[dcmt+]
sau96I
avaII
sauI mnlI sfaNI
1001 AGGTCCAGGA GGAAGAGGC ATCAAGTATA AGTTGAAGT CTACGAGAG AGAAGACTAAC AGGAGATGC TTTCAGATTCT TCTGCTCCCT TCCTAAAGCT
TCCAGGTCTCT CTTTTTCCG TAGTTTCATAT TCAAACTTCA GATGCTCTTC TTCTGATTG TCCTCTACG AAAGTTCAG AGACGAGGGG AGGATTTTCA
*END DFR

styI
bsaJI
sau3AI
nlaIII
styI
ncoI
dsal bsmFI
ppu10I
nslI/avaIII
1101 ATGCATTTT ATAGACCAT GGCACCTTTT CTGCTTTAG ATCCCTTGG CTTCGTTAGA AGCAGCTAC AATTATACA TAACCTTATG TATCATACAC
TACGTAAAAA TATTCTGTA CCTGTGTA CCTGTGTA GACCGAAATC TAGGGGAAC GAAGCAATCT TGCCTGATG TTAATTATCT ATTGGAATAC ATAGTATGTC

sau96I
avaII
asuI
scrFI
mvaI
ecorII

FIG. 48D

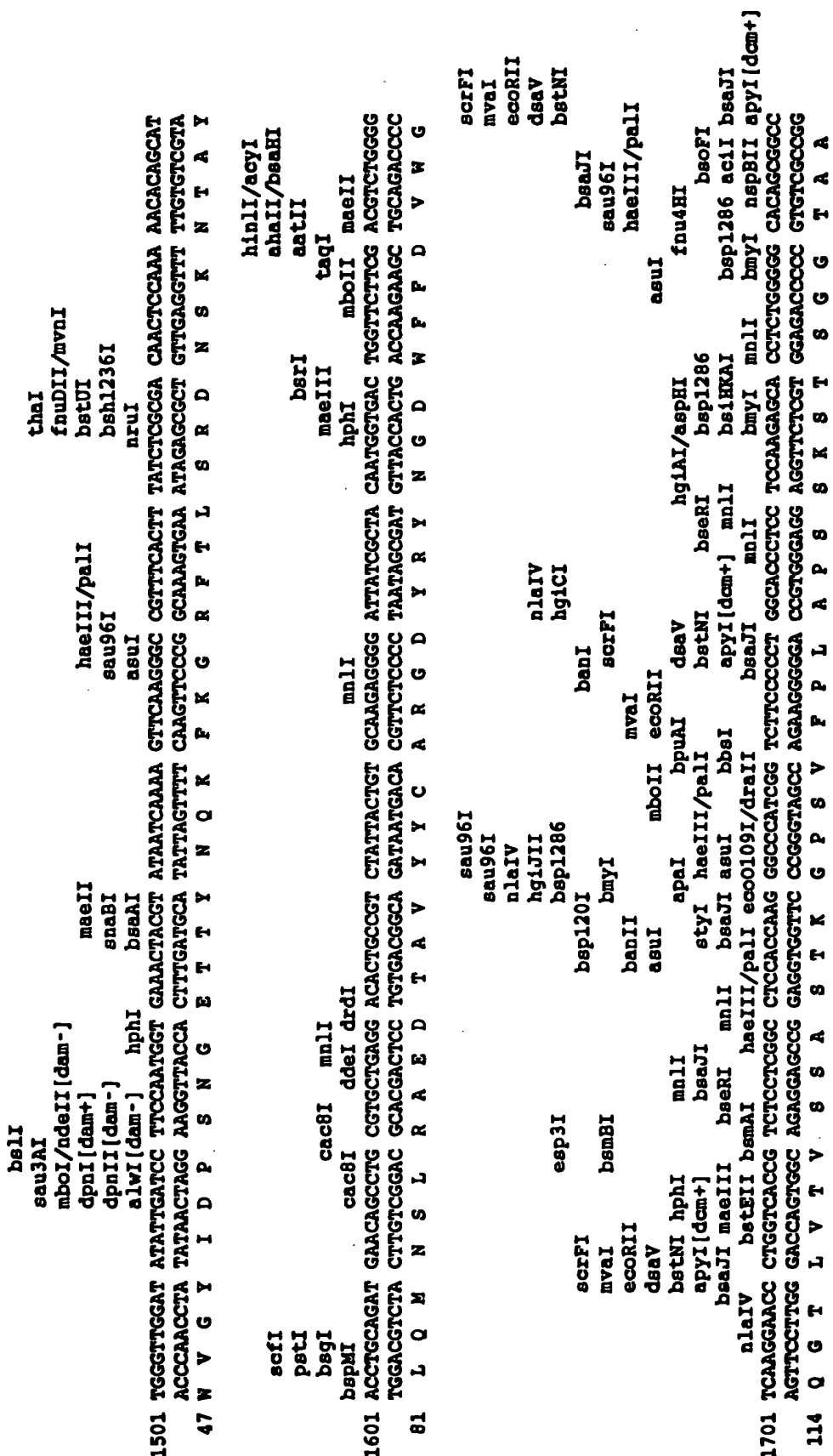


1201 ATACGATTTA GGTGACACTA TAGATAACAT CCACTTTGCC TTCTCTCCA CAGGTGTCCA CTCCAGGTC CAACTGCACC TCGTTCTAT CGATTGANTT
TATGCTAAAT CCACTGTAT ATCTATTGTA GGTGAACCG AAGAGAGGT GTCCACAGT GTCCACAGT GTTGAACGTTG AGCCAGATA GCTACTTAA
seq from PRK6425VH: Cla-AvriI^

1301 CCACCATGGG ATGTCATGT ATCATCTTT TTCTAGTAGC AACTGCACT CGAGTACAT CAGAGTTCA GCTAGTGCAG TCTGGCGTG CCGTGTGCA
GGTGTACCC TACCAGTACA TAGTAGGAA AAGATCATCG TTGACGTGA CCTATGTAA GTCTCAAGT CGATCACGTC AGACCCGAC CCGACACGT
E V Q L V Q S G G G L V Q

1401 GCCAGGGGC TCACTCGGT TGTCTGTGC AGTTCTGCG TACTCTTCT CGAGTCACTA TATGCTAGT GTCCGTGAG CCCCCTGTA GGGCTGGAA
CGTCCCGG AGTGAGGCA ACAGGACAG TCGAGACCG ATGAGGACG GCTCAGTAT ATACGTACC CAGCAGTCC GGGGCCCAT CCCGACCTT
14 P G G S L R L S C A A S G Y S F S S H Y M H W V R Q A P G K G L E

FIG. 48E



scrFI
 mvaI
 ecoRII
 dsav
 bstNI
 bsaJI
 sau96I
 haeIII/pali
 asuI
 fnu4HI
 bsoFI
 bsp1286 aciI bsaJI
 bmyI bmyI bmyI
 CCTCTGGGG CACAGGGCC
 GTGTGCGCG
 T A A
 S G G T S K S T
 A P S A P S V F P L
 GAGACCGCC GTGTGCGCG
 AGGTCTTGG GACCAGTGG AGAGAGGCC GAGGTGGTTC CCGGTAGCC AGAAGGGGA CCGTGGGAG AGGTCTCGT GAGACCGCC GTGTGCGCG
 114 Q G T L V T V S S A S T K G P S V F P L A P S S K S T S G G T A A



```
scrFI      hlnPI      hglAI/aspHI      hspI
nval       nlaIV      neri      bsp1286      nspI
ecorII     kasi      hlnII/acyI      bmyI      hpall
econI      hgiCI      haeII      fnu4HI      scrFI
dsav       bani      ahaII/bsaHI      acII apaLI/snoI      dsav      nclI
bstNI      ddel tthIIII/aspI      ddel hhai/cfoI      nsp8II      alw44I/snoI      caulI      scfI
bsaFI      baII      cfr10I/bsrFI      bsaWI      ageI      tthIIII/aspI      GAACCGGTGA      CGGTGTGTG      GAACCTGAGG      GCCTTGACCA      CGCGGTGCA      CACCTTCCC      GCTGTCTTAC
1801 CTGGGCTGCC      TGGTCAAGGA      CTACTTCCC      GAACCGGTGA      CGGTGTGTG      GAACCTGAGG      GCCTTGACCA      CGCGGTGCA      CACCTTCCC      GCTGTCTTAC
GACCGGAGG      ACCAGTTCT      GATGAAGGG      CTGGCCACT      GCCACAGCAC      CTGAGTCCG      CGGACTGCT      CGCGGTGCA      CACCTTCCC      GCTGTCTTAC
147 L G C L V K D Y F P E P V T V S W N S G A L T S G V H T F P A V L Q
bali      bsp1286      maelII      hphi      bmyI      mnlI      bbvI      ddel
fnu4HI     bsoFI      fnu4HI     nlaIV      hgiCI      bani      tfII      hinfI
bsaFI      bmyI      mnlI      bbvI      ddel      bsp1286      maelII      hphi      bmyI      mnlI      bbvI
bsu36I/mstII/sauI      ddel      bsp1286      maelII      hphi      bmyI      mnlI      bbvI      ddel
1901 AGTCTCAGG      ACTTACTCC      CTCAGCAGG      TGGTACTGT      GCCTCTAGC      AGCTGGGCA      CCCAGACCTA      CATCTGCAAC      GTGAATCACA      AGCCAGCAA
TCAGGAGTCC      TGAGATGAGG      GAGTGTGCG      ACCACTGACA      CGGAGATCG      TCGAACCGT      GGTCTGAT      GTAGAGTTG      CACTAGTGT      TCGGCTGTT
181 S S G L Y S L S S V V T V P S S S L G T Q T Y I C N V N H K P S N
scrFI      hgiJII      bsp1286      bmyI      bani      maelII      mnlI      bbvI      ddel
nval       nlaIV      bstNI      nlaIV      bsaJI      bsmFI      bbsI      mnlI
ecorII     dsav       bsaJI      bsmFI      bbsI      mnlI
scrFI      mval       asuI      ecorII     dsav       bstNI      nlaIV      bsaJI      bsmFI      bbsI      mnlI
2001 CACCAAGTG      GACAGAAAG      TTGAGCCCA      ATCTGTGAC      AAAACTACA      CATGCCACC      GTGCCAGCA      CCTGACTCC      TGGGGGACC      GTAGTCTTC
GTGGTTCAC      CTGTTCTTC      AACTCGGTT      TAGAACACTG      TTTGAGTGT      GTAGAGTGT      GAGTGTGAGG      ACCCCCTGG      CAGTCAGAG
214 T K V D K K V E P K S C D K T H T C P P C P A P E L L G G P S V F
abdl/eam1105I
sau96I
avaII
scrFI
mval
asuI
ecorII
dsav
bstNI
nlaIV
bsaJI
bsmFI
bbsI
mnlI
```

FIG. 48G



2101 sau96I
nlaIV
mspI
hpaII
scrFI
ncII
dsav
sau3AI aValI nlaIII
mboI/ndelI[dam-]
nlaIII cauII mnlI nspHI
rcal dplnI[dam+] ddelI mali
mnlI dplnI[dam-] eco8II maelII
styI mnlI bspHI[dam-] sauI bsu36I/mstII/sauI
earI/ksf32I bsaJI mslI bspHI[dam-] GGACCCCTGA GGTCAATGC GTGGTGGTGC ACCTGAGCCA
2301 CTCTTCCCC CAARAACCAA GGACACCCCTC ATGATTCTCC GGACCCCTGA GGTCAATGC GTGGTGGTGC ACCTGAGCCA
GAGAAGGGG GTTTGGGT CTGTGGGAG TACTAGAGG CTGTGGGAGT CCAGTGATCG CACCACCAAC TGCATCTGGT GCTTCTGGGA CTCCAGTCA
247 L F P P K P K D T L M I S R T P E V T C V V V D V S H E D P E V K F
acII
thaI
fnuDII/mvnl
bstOI
bsh1236I
sacII/sstII
nspBII
kspl
dsal
bsaJI
maelI
rsal
acII
fnu4HI mnlI
bsaJI
maelI
rsal
csp6I
maelI
bsaJI
csp6I
hphI
hgaI mnlI
2201 TCAACTGTA CGTGGAGGC GTGAGGTGC ATAAATCCAA GACAAAGCCG CGGGAGGAGC AGTACAACAG CACGTACCCT GTGGTCAGCG TCCTCACCGT
AGTTGACCAAT GCACCTGCCG CACCTCCACG TATTACGGT CTGTTGGC GCCTCTCTG TCATGTTCTC GTGATGCGA CACCAAGTCC AGGAGTGCGA
281 N W Y V D G V E V H N A K T K P R E E Q Y N S T Y R V V S V L T V
scrFI
mval
ecoRII
dsav
ecoNI bstNI bsrI
belI apyI[dam+]
2301 CCTGCACCAAG GACTGGCTGA ATGGCAAGGA GTACAGTGC AGGTCTCCA ACAAGCCCT CCCAGCCCC ATCGAGAAA CCATCTCCAA AGCCAAGGG
GGACGTGGTCT CTGACCGACT TACCGTCTCT CATGTTACG TTCCAGAGGT TGTTCGGGA GGTTCGGGG TAGCTCTTTT GGTAGAGGTT TCGGTTTCCC
314 L H Q D W L N G K E Y K C K V S N K A L P A P I E K T I S K A K G
fnu4HI
bsaJI
bbvI
bsaJI

FIG. 48H

scrFI
ncII
mepI
hpaII
dsaV
cauII
xmaI/psaI
smaI
scrFI
ncII
dsaV
cauII
rseI
fokI
csp6I
bsp1407I/barGI bslI auaI earI/ksp632I
avaI
2401 CAGCCCGAG AACCAAGGT GTACACCTG CCCCATCC GGGAGAGAT GACCAAGAC CAGGTACGCC TGACTGCTT GGTCAAAGCC TTCTATCCCA
GTGGGGCTC TTGGTGTCCA CATGTGGGAC GGGGGTAGGG CCCTTCTCTA CTGGTTCTTG GTCCAGTCGG ACTGACGCGA CCAGTTTCCG AAGATAGGCT
347 Q P R E P Q V Y T L P P S R E E M T K N Q V S L T C L V K G F Y P S
mspI
hpaII
fnu4HI
bsoFI
bsrDI bsvI
2501 GCGACATCC CGTGGAGTGG GAGAGCAATG GCGAGCGGA GAACAACACTAC AAGACCACGC CTCCTGCTCT GACTCCGAC GGCTCCTTCT TCCCTACAG
CGCTGTAGCG GCACCTCACC CTCTCGTTAC CGGTGGGCTT CTGTGTGATG TTCGTGGTGG GAGGGCACGA CTTGAGGCTG CCGAGGAGGA AGGAGATGTC
361 D I A V E W E S N G Q P E N N Y K T T P P V L D S D G S F P L Y S
pleI
hinfI
nlaIV mboII scfI cac8I
mli
mboII
414 K L T V D K S R W Q Q G N V F S C S V M H E A L H N H Y T Q K S L
dsal
hphI
aluI bsaJI
2601 CAAGCTCACC GTGACAAGA GCAGGTGGCA GCAGGGGAAC GTCTTCTCAT GCTCCGTGAT GCATGAGGCT CTCACACACC ACTACACGCA GAAGAGCCTC
GTTGAGTGG CACCTGTTCT CGTCCACCGT CGTCCCTTG CAGAGAGTGA CGAGGCACTA CGTACTCCGA GACGTGTGG TGAATGCGT GTTCTGGAG
414 K L T V D K S R W Q Q G N V F S C S V M H E A L H N H Y T Q K S L
mboII
bpuAI
maeII
fnu4HI
bsoFI
bspMI bsvI
asp700
nlaIII
sfanI mli
ppuOI
nslI/avaIII
nlaIII
sapi
mboII mli
earI/ksp632I
GAAGAGCCTC
GTTCTGGAG

FIG. 48I



```

scrFI      sau96I      acII      haeIII/palI      aluI      maeIII
ncII      fnu4HI      asuI      bsoFI      nlaIII      fnu4HI      bsoFI      bbVI
mspI      taqI      pleI      rmaI      salI      scfI      maeI      hincII/hindII      aluI      maeIII
hpaII      maeI      hincII/hindII      pstI      sau96I      hincI      pti      haeIII/palI      aluI      haeIII/palI      maeIII
dsav      haeIII/palI      asuI      bfaI      accI      bspMI      hindIII      bgII      bsaJI      maeIII
bmaI      belI      cauII      AGTGGGACGG      CCTAGAGTC      GACCTGCAGA      AGCTTGCGCG      CCATGGCCCA      ACTTGTTTAT      TGCAGCCTTAT      AATGGTTACA
2701      TCCTGTCTC      CGGGTAAATG      AGTGGGACGG      CCTAGAGTC      GACCTGCAGA      AGCTTGCGCG      CCATGGCCCA      ACTTGTTTAT      TGCAGCCTTAT      AATGGTTACA
AGGACAGAG      GCCCATTTAC      TCACCGTGGC      GGGATCTCAG      CTGGACGTCT      TCGNACCGGC      GSTACCGGCT      TGAACAAATA      AGTCGAAATA      TTACCAATGT
447      S      L      S      P      G      K      O

sfanI      apol      nlaIII      aluI      (dam-)
2801      AATAAAGCAA      TAGCATCACA      AATTTCACAA      ATAAAGCAAT      TTTTCACTG      CATTCAGTT      GTGGTTGTC      CAAATCATC      AATGTATCTT      ATCATGCTG
TTATTTCGTT      ATCGTAGTGT      TTAAAGTGTT      TATTTCGTAA      AAAAGTGAC      GTAGATCAA      CACCAACAG      GTTTGAGTAG      TTACATAGNA      TAGTACAGAC

sau3AI      mboI/ndeII      (dam-)      nlaIII      aluI      (dam-)
dpmI      (dam+)      maeI
dpmII      (dam-)      bmaI      bfaI
pvuI/bspCI      maeI
mori      xmaI
bsiEI      maeI
taqI      (dam-)      tru9I      raeI
clal/bsp106      (dam-)      nlaIV
bspDI      (dam-)      maeI      kplI
sau3AI      xmiI      hincPI      dsal      haeIII/palI      hgiCI
mboI/ndeII      (dam-)      hhal/cfoI      nlaIII      bani
dpmI      (dam+)      asp700      hhaI/asnI/vspI      bsaJI      asp718      mnII
dpmII      (dam-)      asel/asnI/vspI      bsaJI      acc65I      ddeI      acII
2901      GATCGATCGG      GAATTAATTC      GCGGAGCAC      CATGGCCTGA      AATAACCTCT      GAAAGAGGAA      CTTGTTAGG      TACCTTCTGA      GCGGAAAGA      ACCATCTGT
CTAGCTAGCC      CTTAATTAAG      CCGCGTGTG      GTACCGGACT      TTATTGGAGA      CTTTCTCTT      GAACCAATCC      ATGGAAGACT      CCGCTTCT      TGGTAGACAC
```

FIG. 48J

3001 GAATGTGTGT CAGTTAGGGT GTGGAAGTCC CCAGGGCTCC CCAGCAGGCCA GAAGTATGCC AAGCATGCCAT CTCATATTAGT CAGCAACCAG GTGTGGAAG
CTTACACACA GTCAATCCCA CACCTTCAG GGTCCGAGG GGTGCTCCGT CTTCATACGT TTCTACGTA GAGTTAATCA GTGTTGGTC CACACCTTTC

3101 TCCCCAGGCT CCCAGCAGG CAGNAGTATG CAAGCATGC ATCTCAATTA GTCAGCAACC ATAGTCCGC CCCTAATCC GCCATCCG CCCCTAATC
AGGGGTCCGA GGGTCTGTC GTCTTCATAC GTTTCGTACG TAGAGTTAAT CAGTCTTGG TATCAGGGCG GGGATTGAGG CGGTAGGGC GGGGATTGAG

3201 GCGCCAGTTC CGCCCATCTT CGGCCCATG GCTGACTAAT TTTTTTTATT TATGCAGAG CCGAGGCCG CTCGGCTCT GAGCTATTCC AGAAGTAGT
GCGGGTCAAG GCGGTAAGA GCGGGGTAC CGACTGATTA AAAAAATAA ATAGTCTCC GGTCCGCGC GAGCCGAGA CTCGATAAGG TCTTCATCAG

FIG. 48K



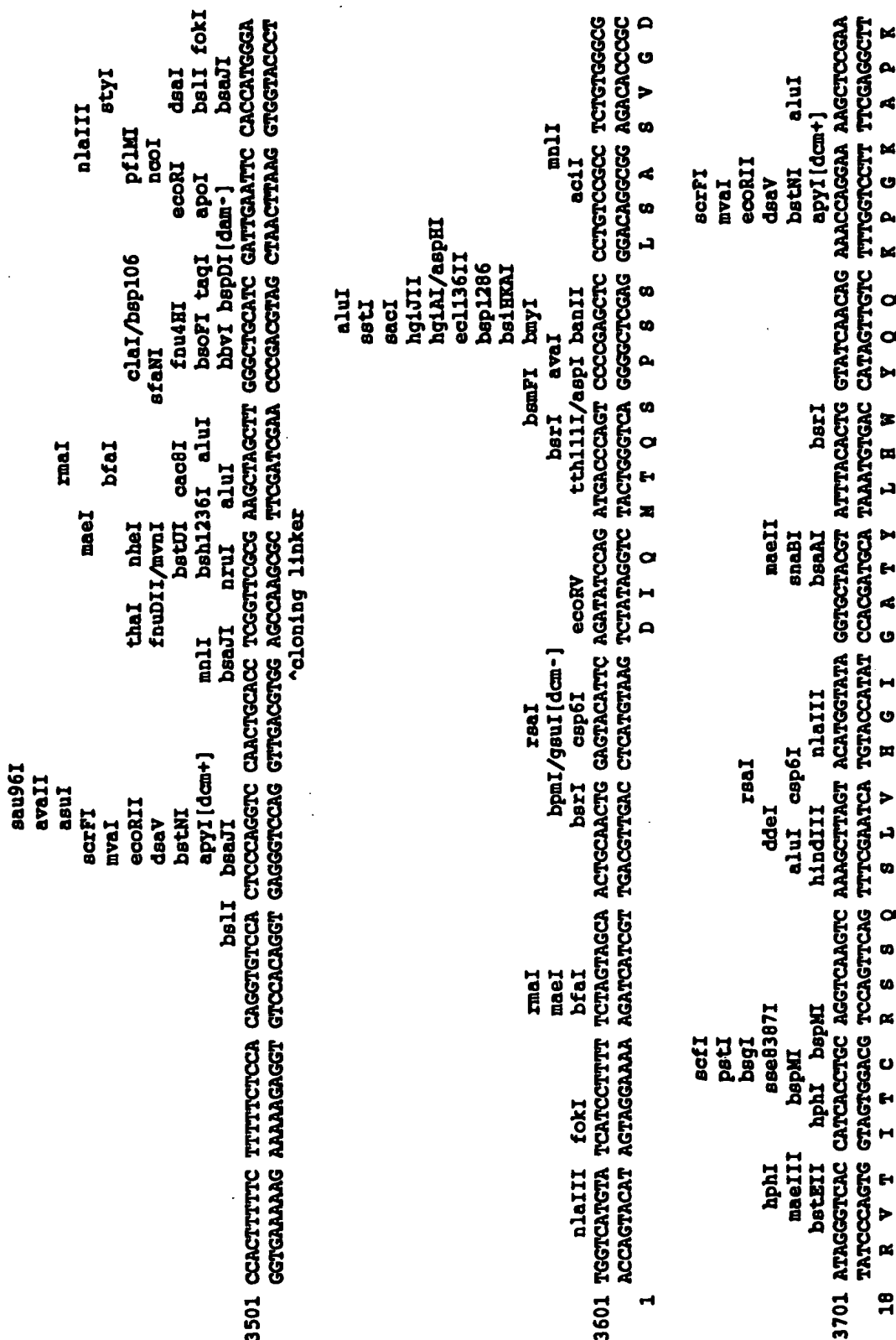
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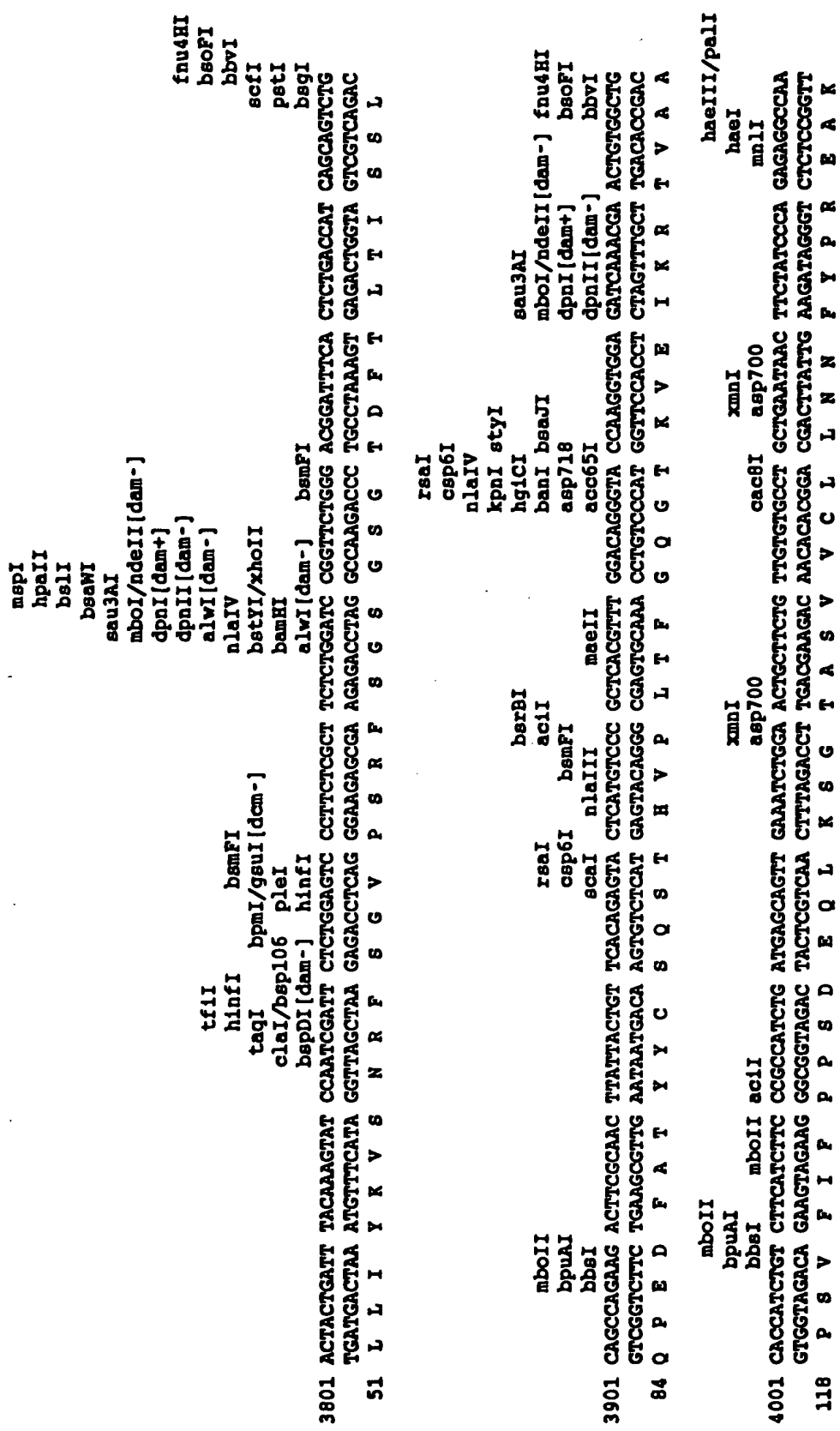
rmaI      scrFI
maeI      nciI
styI      mspI
bsaJI     hpall
blnI      dsav
          haeIII/palI
          mcrI      tfII
          eagI/xmaIII/ecI XI  hinfI
          eaeI      aciI
          cfrI      theI
          bsiEI     fnuDI/mvnI
          mspI cauII  bstDI
          cac8I      bsh1236I
          aluI      hpall
          rmaI      mcrI      tfII
          maeI      eagI/xmaIII/ecI XI  hinfI
          bfaI      eaeI      aciI
          nheI      cfrI      theI
          cac8I      bsiEI     fnuDI/mvnI
          aluI      mspI cauII  bstDI
          mnlI bfaI  hpall      bsh1236I
          mnlI      mnlI      pleI
          mnlI      mnlI      hinfI
3301 AGGAGGCTTT TTTGGAGGCC TAGGCTTTT CAAAGAGCTA GCTTATCCGG CCGGGAACGG TGCATTGGAA CGCGGATTCC CGTGCCCAAG AGTCAGGTAA
TCCTCCGAAA AATCCGAGGC ATCCGAAAC GTTTTTCGAT CGATATAGCC GGCCTTGCC AGCTAACCTT GCGCTAAGG GGCACGGTTC TCAGTCCATT
^seq from pSV1685-6G4VL: AvrII - HindIII frag
          U1 matched splice donar^

          sau3AI
          mboI/ndeII[dam-]
          dpnI[dam+]
          dpnII[dam-]
          alwI[dam-]
          taqI[dam-]
          clai/bsp106[dam-]
          bspDI[dam-]
          sau3AI
          mboI/ndeII[dam-]
          dpnI[dam+]
          dpnII[dam-]
          alwI[dam-]
          foki
          fnu4HI
          bsoFI
          aciI
          thaI
          fnuDI/mvnI tru9I
          bstUI mseI
          bsh1236I aseI/asnI/vspI
          gttAGAACCC GGTACAAATT AATACATAAC CTTTGGATC GATCCTACTG ACACGTGACAT
          CATGCGGAT ATCTCAGATA TCGGGGTGGG GGAACCGAAG CAATCTTGG TATGTATTG GAAACACTAG CTAGGATGAC TGTGACTGTA
          ^sp6 promoter
          ^U2 match
          lariat consensus^
          I96 vH natural lariat restored^

```

FIG. 48L





[illegible]

FIG. 480



```

sau3AI
mboI/ndeII[dam-]
dpmI[dam+]
dpmI[dam-]
pvuI/bspCI
mcrI
bsiEI
taqI[dam-]
claiI/bsp106[dam-]
bspDI[dam-] tru9I
sau3AI mseI
mboI/ndeII[dam-]
dpmI[dam+] xmiI
dpmI[dam-]
dpmI[dam-] asei/asnI/vspI bsaJI
nlaIII alwI[dam-] asp700 hhaI/cfoI nlaIII
4401 TTTTTCACATG CATTCTAGTT GTGGTTTGTG CAAACTCATC AATGTATCTT ATCATGTCTG GATCGATCGG GAATTAATTC GCGCAGCAC CATGGCCTGA
AAAAAGTCAC GTACATCAAA GTTTGAGTAG TTACATAGAA TAGTACAGAC CTAGCTAGCC CTTAATTAAG CCGCGTCTG GTACCGACT
^sv40 origin

rseI
csp6I
nlaIV
kpnI
hgiCI
bani
asp718 mnlI
acc65I ddeI aciI
4501 AATAACTCT GAAGAGGAA CTTGGTTAGG TACCTTCTGA GCGGGAAGA ACCAGCTGTG GAATGTGTGT CAGTTAGGGT GTGGAAGTC CCCAGGCTCC
TTATTGGAGA CTTTCTCCTT GAACCAATCC ATGGAAGACT CCGCCTTCT TGTGCGACAC CTTACACACA GTCAATCCCA CACCTTTCAG GGTCCGAGG

mnlI mnlI
bsmI bfaI
rmaI
maeI
bsmI bfaI
4601 CCAGCAGGCA GAAGTATGCA AAGCATGCAT CTTCAATTAGT CAGCAACCAG GTGTGGAAG TCCCGAGGT CCCAGCAGG CAGAAGTATG CAAAGCATGC
GGTCGTCCGT CTTACATCGT TTGTAGCTGA GAGTTAATCA GTCTTGGTC CACACCTTTC AGGGTCCGA GGGGTCTGCC GTCTTCATAC GTTCTGTACG

rseI
csp6I
nlaIV
kpnI
hgiCI
bani
asp718 mnlI
acc65I ddeI aciI
4501 AATAACTCT GAAGAGGAA CTTGGTTAGG TACCTTCTGA GCGGGAAGA ACCAGCTGTG GAATGTGTGT CAGTTAGGGT GTGGAAGTC CCCAGGCTCC
TTATTGGAGA CTTTCTCCTT GAACCAATCC ATGGAAGACT CCGCCTTCT TGTGCGACAC CTTACACACA GTCAATCCCA CACCTTTCAG GGTCCGAGG

mnlI mnlI
bsmI bfaI
rmaI
maeI
bsmI bfaI
4601 CCAGCAGGCA GAAGTATGCA AAGCATGCAT CTTCAATTAGT CAGCAACCAG GTGTGGAAG TCCCGAGGT CCCAGCAGG CAGAAGTATG CAAAGCATGC
GGTCGTCCGT CTTACATCGT TTGTAGCTGA GAGTTAATCA GTCTTGGTC CACACCTTTC AGGGTCCGA GGGGTCTGCC GTCTTCATAC GTTCTGTACG
```

FIG. 48P

4701 ATCTCAATTA GTCAGCAACC ATATGCCCGC CCCTAACTCC GCCATCCCG CCCTAACTC CGCCAGTTC CGCCCATCTT CCGCCCATG GCTGACTAAT
TAGAGTTAAT CAGTCGTTGG TATCAGGGCG GGGATTGAG GGGGATTGAG CGGGTCAAG GCGGGTAAAG GCGGGGTAC CGACTGATTA

4801 TTTTATTAT TATGCAGAGG CCGAGGCCG CTCGGCTCT GAGCTATTCC AGAGTAGTG AGGAGGCTT TTTGGAGGCC TAGGCTTTTG CAARAAGCTG
AAAAAATAA ATACGTCCTCC GGCTCCGGCG GAGCCGGAGA CTCGATAAGG TCTTCATCAC TCCTCCGAAA AAACCTCGG ATCCGAAAC GTTTTCGAC
start pUC118

4901 TTACCTCGAG CGSCCGCTTA ATTAAGCGCG GCCATTAAA TCTGTCAGT AACAGCTTGG CACTGCGCT CAGTTTACAA CGTCGTGACT GGGAAAOCC
AATGGAGTC GCGCGCGAAT TAATTCGCG CGGTAAATT AGCAGTCCA TTCTCGAACC GTGACGGCA GCAAAATGTT GCAGCACTGA CCTTTTGGG
*linearization linker inserted into HpaI site

FIG. 48Q

[illegible]

FIG. 48R

[illegible]

FIG. 48S

[illegible]

FIG. 48T



6201 CACGAGTGG TTACATCGAA CTGGATCTCA ACAGCGGTAA GATCCTTCAG AGTTTCGCC CCGAAGACG TTTTCCAATG ATGAGCACTT TTAAGTTCT
GTGCTCACCC AATGTAGCTT GACCTAGAGT TGTCGCCATT CTAGGAACCTC TCARAAGCGG GGCTTCTGCT AAAGGTTAC TACTCGTGAA AATTTCAAGA
sau3AI nspBII sau3AI mboI/ndeII[dam-] maeII
mboI/ndeII[dam-] pep1406I
dpnI[dam+] xnnI
bstYI/xhoII dpnII[dam-] asp700
berI dpnII[dam-] mboII
alwI[dam-] bmyI ahaIII/draI
bssI maeIII taqI alwI[dam-] aciI btyI/xhoII
6301 GCTATGTGGC GCGGTATTAT CCGGTGATGA CGCGGGGCAA GAGCACTCG GTGCGCGCAT ACACATTCTT CAGATGACT TGGTTAGTA CTCACCAGTC
CGATACACG CGCATATAA GGGCACTACT CGCGCCCGTT CTCGTTGAGC CAGCGCGGTA TGTGATAAGA GTCTACTGA ACCAATCAT GACTGGTGCTAG
scrFI
aciI
thaI
fnuDI/mvnI
bstUI
bsh1236I
hinPI
hhaI/cfoI
hinII/acyI
hgaI caulI
ahaII/dsaHI
bogi bseI bsoFI
mcrI fnu4HI
aciI
ddei
rsal
csp6I
bsrI
scaI hphI maeIII
6401 ACAGAAAAGC ATCTTACGGA TGGCATGACA GTAGAGAAAT TATGCACTGC TGCCATNACC ATGAGTGATA AACTGCGGC CAATCTACTT CTGACACGGA
TGCTTTTCG TAGAATGCCCT ACCGTACTGT CATCTCTTA ATAGTCACG ACGGTATTGG TACTCACTAT TGTGACGCCG GTTGAATGAA GACTGTTGCT
sfaNI foki nlaIII
fnu4HI
bsoFI
bbvI mslI nlaIII
haeIII/palI
eaeI
cfrI
fnu4HI
bsoFI
aciI
sau3AI
mboI/ndeII[dam-]
dpnI[dam+]
dpnII[dam-]
pvuI/bspCI
mcrI
bseI
6501 TCGGAGGACC GAAGGAGCTA ACCGCTTTT TGCACAACAT GGGGATCAT GTAACTCGCC TTGATGTTG GGNACCGGAG CTGAATGAAG CCATACCAAA
AGCCTCCTGG CTTCCTCGAT TGGCGAAAAA ACGTGTGTGA CCCCCTAGTA CATGACCGG AACTAGCAAC CCTTGGCCTC GACTTACTTC GGTATGGTTT
sau96I
avaII
aeuI
mnlI
sau3AI maeIII
mboI/ndeII[dam-]
dpnI[dam+]
dpnII[dam-]
nlaIII
alwI
aciI
sau3AI nlaIV
mboI/ndeII[dam-] aluI
dpnI[dam+] hpaII
dpnII[dam-] bsaWI

FIG. 48U



6601 CGACGAGCGT GACACCAAGG TCCAGCAGC AATGCAACA ACCTTGGCA AACTATTAACT TGGCGAATA CTACTCTAG CTTCGGGCA ACATTAATA
GCTGCTGCA CTGCTGCTGCT ACCTGCTGCT TTACCTGCTGCT TGCACGCTGCT TGCATTAATTG ACCGCTTGT GATGAGATC GAAGGCGCT TGTAAATTAT
6701 GACTGGATGG AGGCGGATAA AGTTCAGCA CCACCTTCTGC GCTCGGCCCT TCCGCTGGC TGGTTTATG CTGATAAATC TGGAGCGGT GAGCGTGGGT
CTGACCTACC TCCGCTATT TCAACGCTCT GGTGAAGACG CGAGCCGGA AGGCGGACG ACCAATAAC GACTATTAG ACTCGGCCA CTGCGACCCA
6801 CTCGCGGAT CATTGAGCA CTGGGGCCAG ATGGTAAGCC CTCGCTATC GTAGTATCT ACACGAGGG GAGTCAGGA ACTATGGATG AACGAATAG
GAGCGCATA GTAACGCTCT GACCCCGTC TACCATTGG GAGGCGATG CATCATAGA TGTGCTGCC CTCAGTCCCT TGATACCTAC TTGCTTATC
6901 ACAGATCGCT GAGATAGTG CCTCACTGAT TAAGCAATGG TAACGTGTCAG ACCAAGTTA CTCATATA CTCTAGATTG ATTTAACT TCATTTTAA
TGTCTAGCA CTCTATCCAC GGAGTGACTA ATTGTAACC ATTGACAGTC TGGTTCAAT GAGTATAT GAAATCTAC TAAATTTGA AGTAAATTT
7001 TTTAAAGGA TCTAGTGAA GATCCTTTT GATAATCTCA TGACCAAAAT CCCTTAACGT GAGTTTCTG TCCACTGAGC GTCAGACCCC GTAGAAAGA
AAATTTCTCT AGATCCACTT CTAGGAAA CTATTAGAT ACTGGTTTGA GGAATGCA CTCGAGGCA AGGTGACTCG CAGTCTGGG CATCTTTCT

FIG. 48V

[illegible]

FIG. 48W

7501 TGAGCATGGA GAAGCGCCA CGCTTCCCGA AGGGAGAAG CGGACAGGT ATCCGGTAAG CGGCAGGTC GGAACAGGAG AGCGACGAG GGAGCTTCCA
 ACTCGTAACCT CTTTCGGGCT GCGAAGGGCT TCCTCTTTTC CGCCTGTCCA TAGGCCATTC GCCGTCCAG CCTTGTCTC CTCTGAAGGT
 hinfI fnu4HI mspI hpaII bsaBI hhaI/cfoI aluI apyI[dcmt+]
 hhaI/cfoI bsoFI bsaBI hinfI mnlI hhaI/cfoI aluI apyI[dcmt+]
 haeII acII bsaWI acII
 7601 GGGGAAACG CCTGTATCT TTATCTCCT CTCGGGTTTC GCCACTCTG ACTGTAGCGT CGATTTTGT GATGCTCGTC AGGGGGGCG AGCTATATGGA
 CCCCCTTTGC GGACCATAGA AATATCAGGA CAGCCCAAG CGGTGCGAC TGAACTCGCA GCTAAAACA CTACGAGCAG TCCCCCGGC TCGATATCCT
 haeIII/pali haeIII/pali mnlI drdI hgaI sfaNI nlaIV
 fnu4HI scrFI haeIII/pali
 bsoFI mvaI bslI acII
 acII thal bslI fnuDII/mvni haeIII/pali nspI
 thal bslI bstNI haeIII/pali nspI
 fnuDII/mvni haeIII/pali nspI
 bstUI bsh123EI nlaIV haeI cae8I aflIII
 cae8I bsh123EI nlaIV haeI cae8I aflIII
 7701 AAACGCGAG CAACGCGCC TTTTACGCT TCCTGCGCTT TTGCTGGCCT TTGCTCACA TGTTCTTTCC TGCCTATCC CTGATTCG TGGATAACCG
 TTTTGGGTC GTTCGCGG AAAATGCCA AGGACCGAA AACGACCGA AACGAGTGT ACAAGAAAGG ACGCAATAGG GACTAAGAC ACCTATTGGC
 fnu4HI
 bsoFI
 bvi
 cae8I acII
 bsrBI fnu4HI mcrI hinfI hhaI/cfoI
 acII aluI acII bsoFI bslEI hhaI/cfoI mnlI acII haeII
 7801 TATTACGCC TTTGAGTGAG CTGATACCG TCSCCGCAGC CGACGACCG AGCGACGGA GTCAGTGAGC GAGGAGCGG AAGAGCGCC AATACGCAA
 ATAATGCGG AACTCCTC GACTATGGG AGCGCGTGG CTTGCTGGC TCGCTGGCT CAGTCACTG CTCCTTCGC TTCTCGCGG TTATGCGTTT
 haeII hhaI/cfoI hpaII fnu4HI bsaBI hhaI/cfoI earI/ksp632I
 hhaI/cfoI bsoFI bvi pleI hinfI hhaI/cfoI mnlI acII haeII

FIG. 48X



```

      thal
      fnuDII/mvnl
      betOI
      beh1236I
      hinPI
      hhal/cfoI
      thal
      fnuDII/mvnl          cac8I
      betOI haeIII/palI   aluI
      beh1236I            tru9I pvuII
      balI eaeI tfII aseI/asnI/vspI
      aciI cfrI hinFI mseI nspBII
7901 CCGCCCTCTCC CCGCGCTTG GCCGATTCTAT TAATCCAGCT GGCACGACAG GTTCCCGAC TGGAAAGCGG GCAGTGAGCG CAACGCAATT AATGTGAGTT
      GCGCGAGAGG GCGCGCAAC CCGCTAGTA ATTAGGTGCA CCGTGCTGTC CAAAGGGCTG ACCTTTGCGC CGTCACTCGC GTTGCCTTAA TTACACTCAA
      mnlI
      aciI
      cac8I
      hinPI
      mseI
      tru9I
      maeIII
      bsrI
      acII
      hhal/cfoI
      aseI/asnI/vspI
      scrFI
      mvaI
      ecorII
      dsav
      nlaIV betNI
      hgiCI apyI[dm+]
      banI bsaJI
      mnlI
8001 ACCTCACTCA TTAGGCACCC CAGGCTTTAC ACTTTATGCT TCCGGCTCGT ATGTTGTGTG GAATTGTGAG CGGATAACAA TTTCACACAG GAAACAGCTA
      TGGAGTGAGT AATCCGTGGG GTCCGAATG TGAAATACGA AGGCCGAGCA TACACACAC CTTACACTC GCCTATTGTT AAAGTGTGTC CTTGTGCGAT
      mspI
      hpaII
      acII
      bsrBI
      aluI
```

FIG. 48Y



```
tru9I
mseI
aseI/asnI/vspi
xmni
nlaiI asp700
8101 TGACCATGAT TACGAATTAA
ACTGGTACTA ATGCTTAATT

>length: 8120

aatII(GACGTC): 1690 5947
acc65I(GGTACC): 2969 3967 4529
accI(GTMRAC): 823 1039 2738 4237
aciI(CCGC): 217 229 238 250 260 271 317 422 454 485 574 1385 1795 1871 2248 2250 2758 2982
3167 3179 3188 3200 3210 3221 3267 3372 3404 3449 3686 3949 4021 4318 4542 4727
4739 4748 4760 4770 4781 4827 4910 4914 5070 5127 5153 5166 5203 5217 5220 5248
5275 5680 5699 5741 5751 5790 5979 6026 6125 6234 6311 6355 6476 6522 6713 6804
7166 7175 7310 7420 7541 7560 7687 7715 7806 7827 7834 7877 7901 7911 7967 8070
see hinI

acyI
afII/dfrI(CTTAAG): 786
afIIII(ACRYGT): 932 7758
ageI(ACCGGT): 1833
ahaiI/baehI(GRCGYC): 988 1690 1858 5117 5947 6329
ahaiI/dral(TTTAA): 696 4935 6290 6982 7001
ahdI/eamI105I(GACNNNNNGTC): 2087 6865
alui(AGCT): 5 44 332 386 390 753 1097 1165 1370 1431 1951 2603 2751 2784 3282 3336 3340
3562 3566 3676 3733 3792 4270 4288 4311 4344 4554 4842 4896 4954 5047 5333 5590
5803 5822 6516 6579 6679 7200 7457 7593 7819 7937 8096

alw44I/snoI(GTGCAC): 1876 5651 6198 7444
```

FIG. 48Z

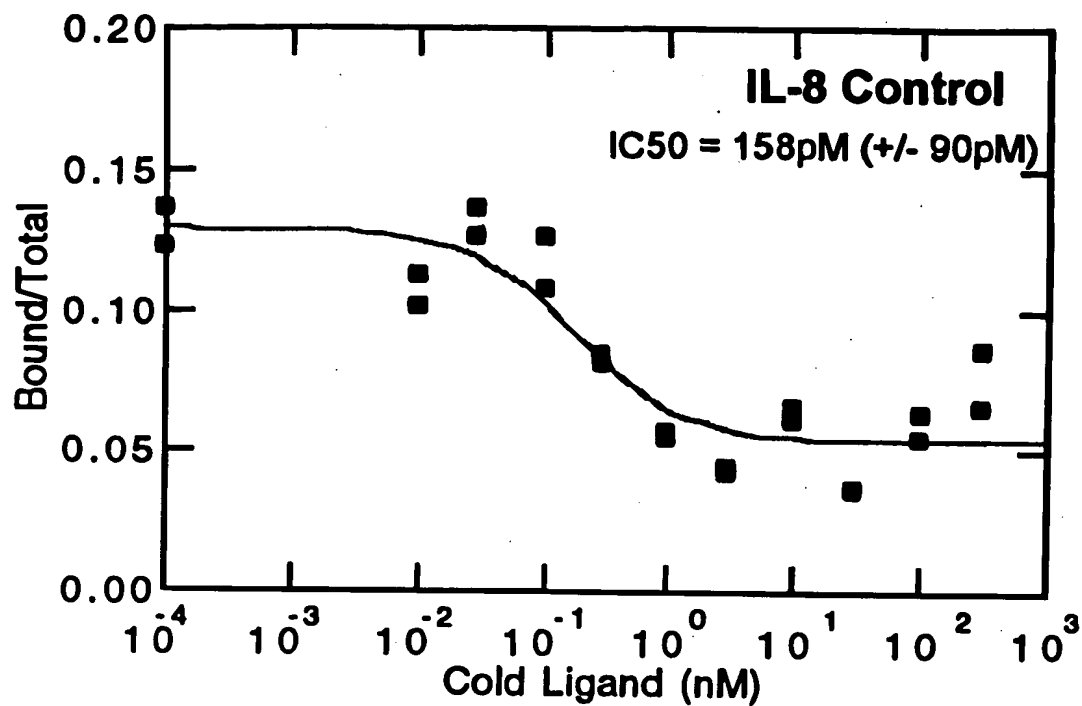


FIG. 49A

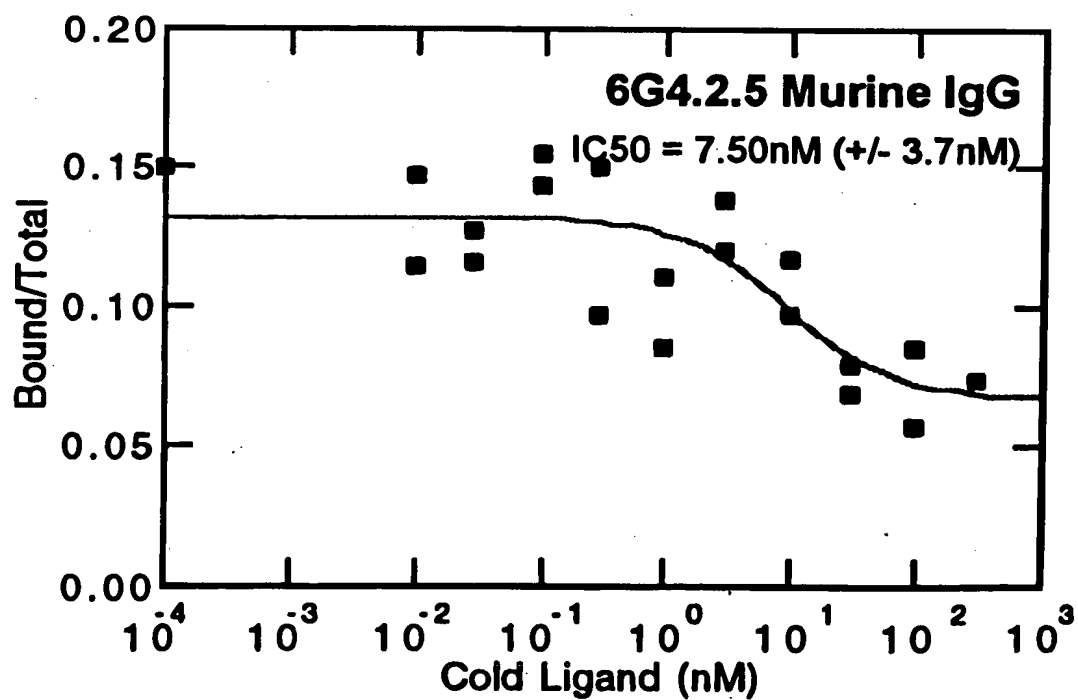


FIG. 49B

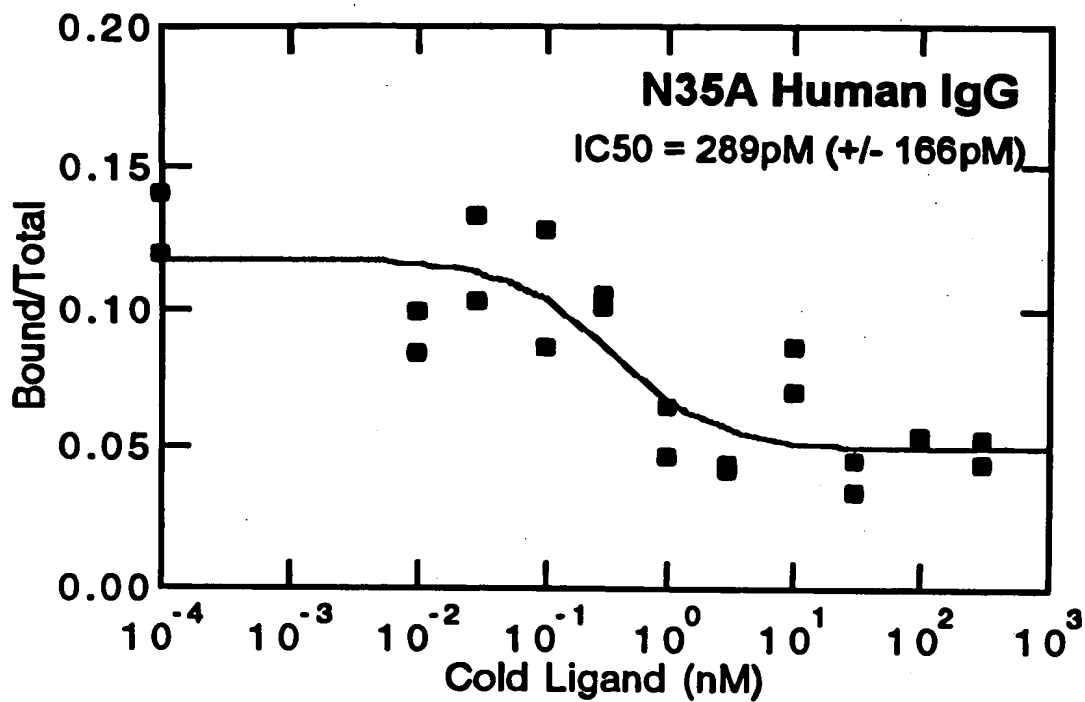


FIG. 49C

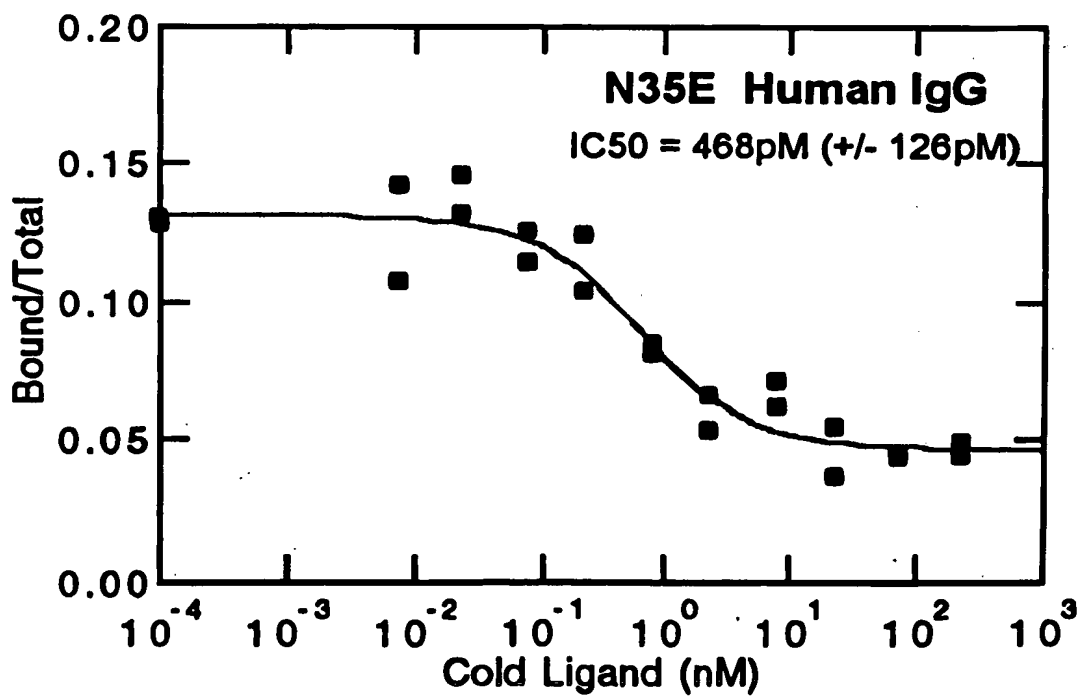


FIG. 49D

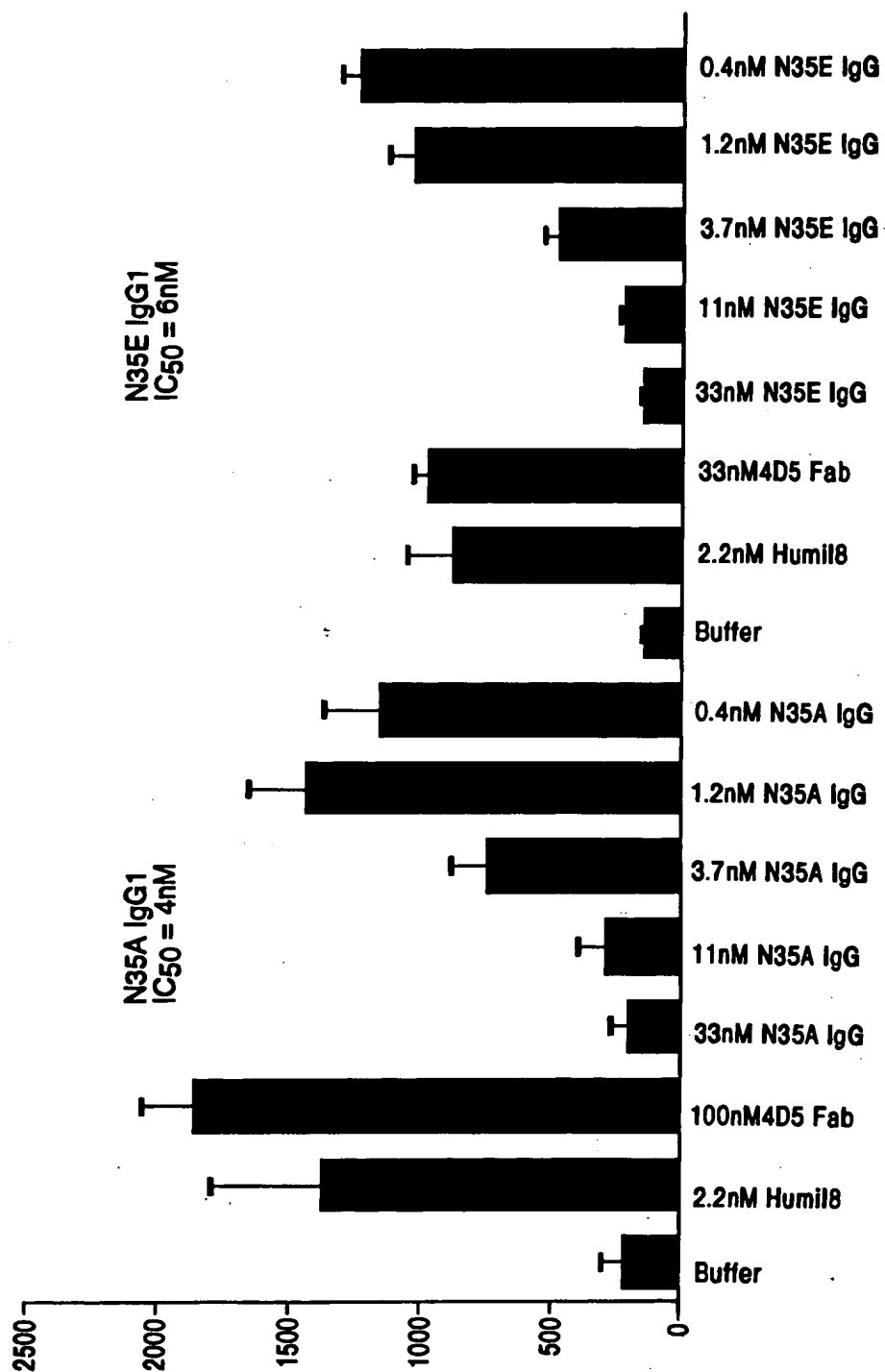


FIG. 50A

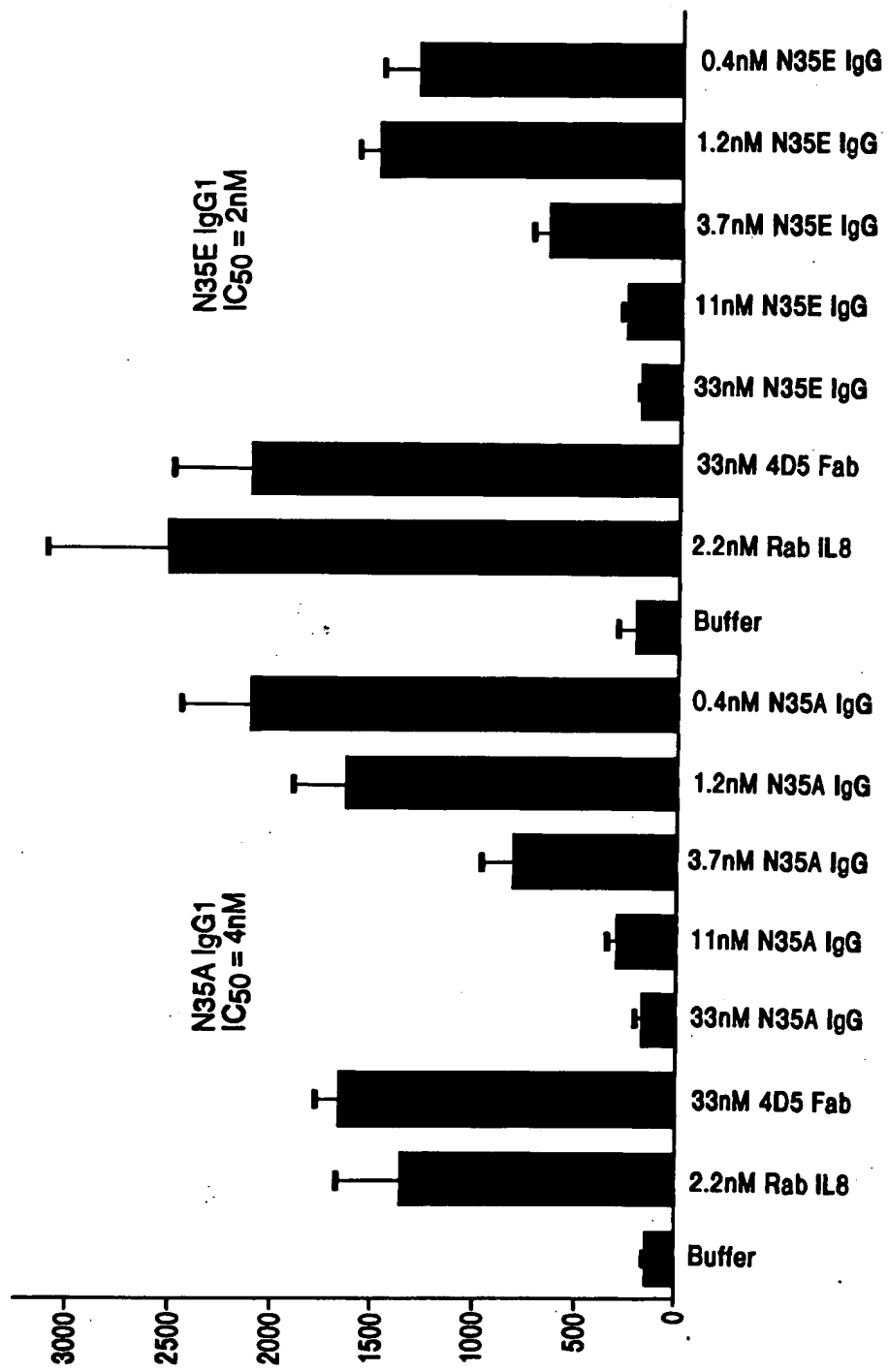
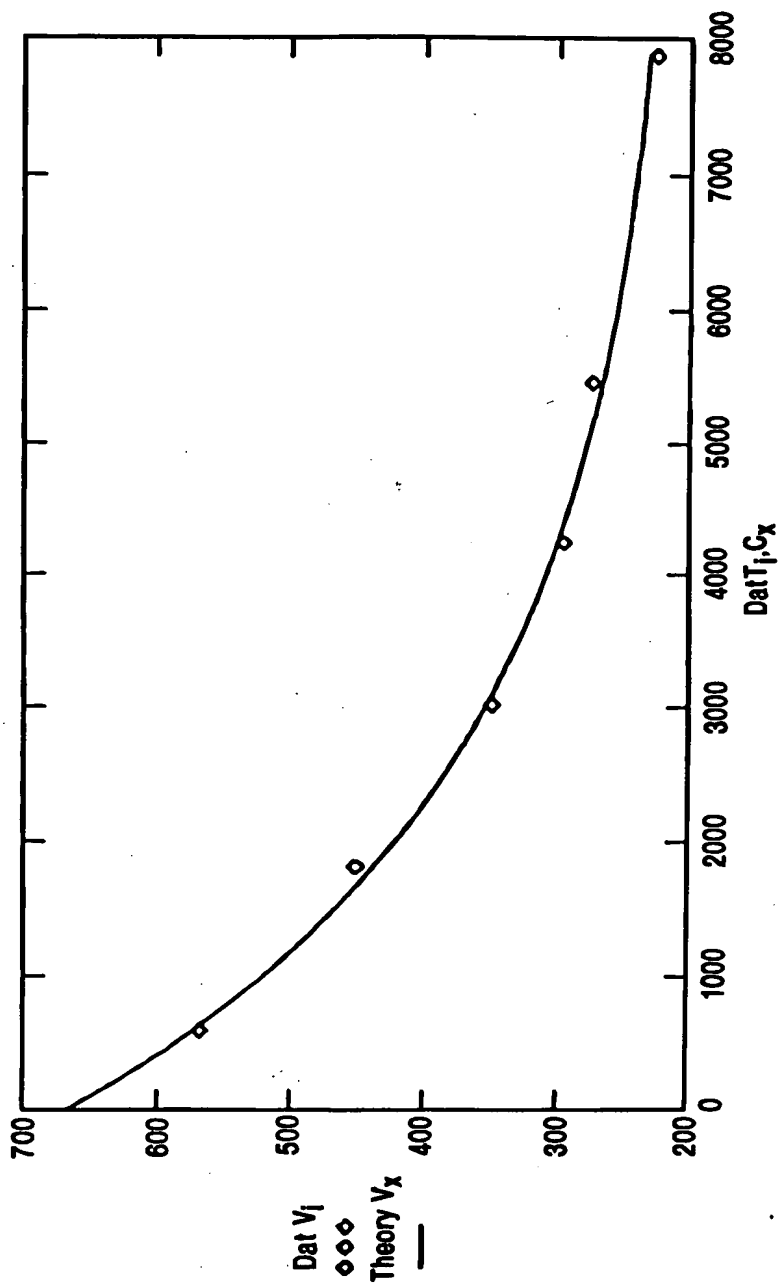


FIG. 50B



Representative Conc versus Time Plot. Shown is the kinetic data for 6G4V11N35A.IgG1

SAMPLE	k_a	k_d	K_d
Murine 6G4.2.5 IgG2a	8.3×10^5	2.9×10^{-4}	350pM
6G4V11N35A-IgG1	8.7×10^5	7.7×10^{-5}	88pM
6G4V11N35E-IgG1	3.0×10^6	1.4×10^{-4}	49pM

FIG. 51

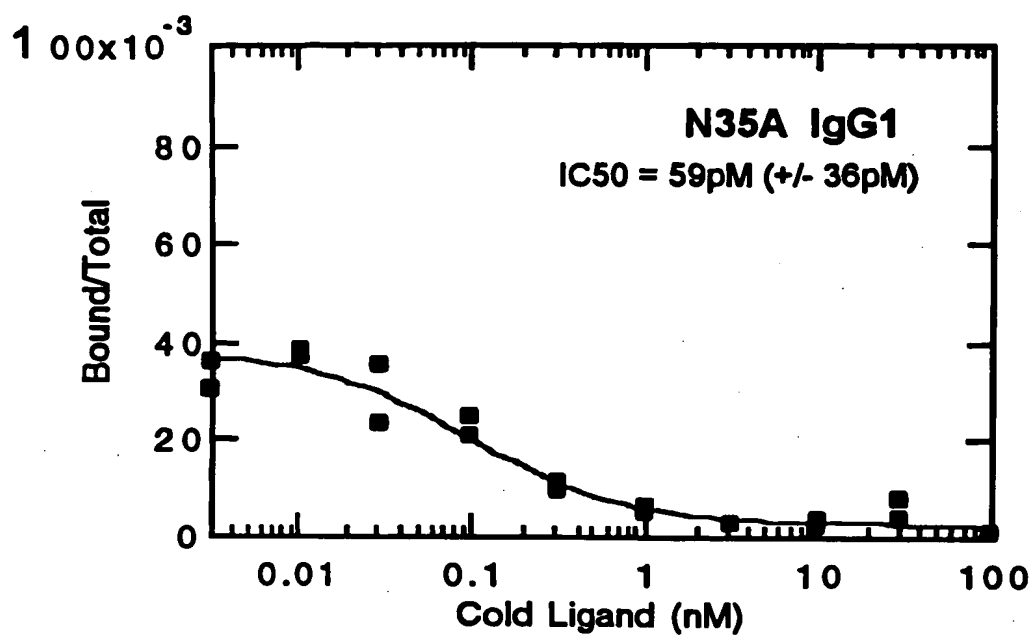


FIG. 52A

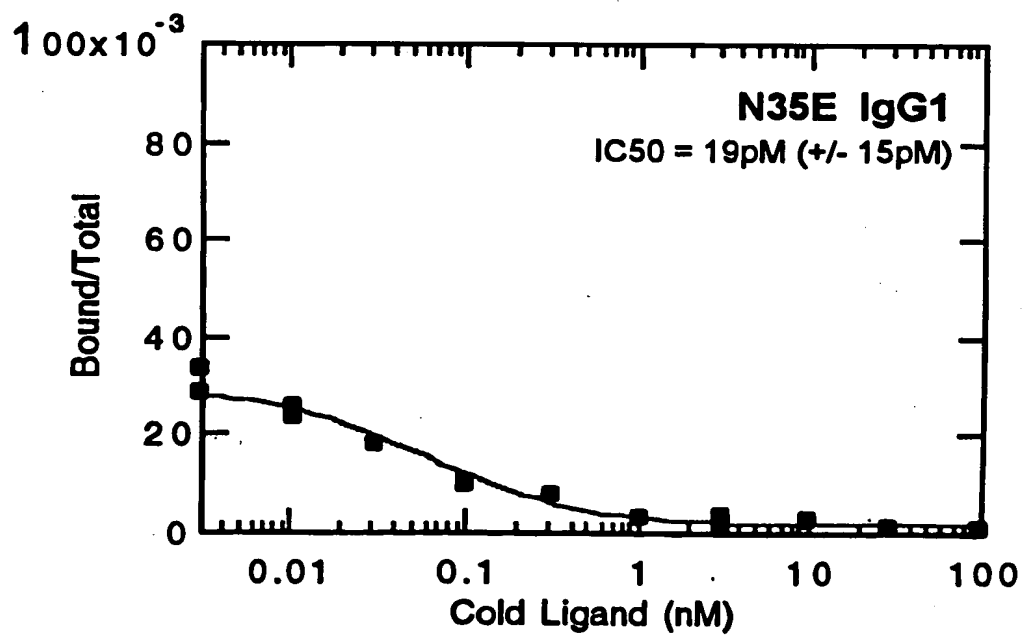


FIG. 52B



781 AAAAGGGTAT CTAGAGGTG AGGTGATTTT ATGAAAAAGA ATATCGCATT TCTTCCTTGCA
TTTTCCCATA GATCTCCAAC TCCACTAAAA TACTTTTCT TATAGCGTAA AGAAGAACGT
-1 M K K N I A F L L A

841 TCTATGTTCG TTTTTTCTAT TGCTACAAAC GCGTACGCTG AGGTTTCAGCT AGTGCAGTCT
AGATACAAGC AAAAAAGATA ACGATGTTTG CGCATGCGAC TCCAAGTCGA TCACGTCAGA
-11 S M F V F S I A T N A Y A E V Q L V Q S

901 GGCGGTGGCC TGGTGCAGCC AGGGGGCTCA CTCCGTTTGT CCTGTGCAGC TTCTGGCTAC
CCGCCACCGG ACCACGTCGG TCCCCCGAGT GAGGCAAACA GGACACGTCG AAGACCGATG
8 G G G L V Q P G G S L R L S C A A S G Y

961 TCCTTCTCGA GTCACTATAT GCACTGGGTC CGTCAGGCCC CGGGTAAGGG CCTGGAATGG
AGGAAGAGCT CAGTGATATA CGTGACCCAG GCAGTCCGGG GCCCATTCCC GGACCTTACC
28 S F S S H Y M H W V R Q A P G K G L E W

1021 GTTGGATATA TTGATCCTTC CAATGGTGAA ACTACGTATA ATCAAAAGTT CAAGGGCCGT
CAACCTATAT AACTAGGAAG GTTACCACTT TGATGCATAT TAGTTTTCAA GTTCCCAGCA
48 V G Y I D P S N G E T T Y N O K F K G R

1081 TTCACTTTAT CTCGCGACAA CTCCAAAAAC ACAGCATACC TGCAGATGAA CAGCCTGCGT
AAGTGAAATA GAGCGCTGTT GAGGTTTTTG TGTCGTATGG ACGTCTACTT GTCGGACGCA
68 F T L S R D N S K N T A Y L Q M N S L R

1141 GCTGAGGACA CTGCCGTCTA TTA CTGTGCA AGAGGGGATT ATCGCTACAA TGGTGA CTGG
CGACTCCTGT GACGGCAGAT AATGACACGT TCTCCCCTAA TAGCGATGTT ACCACTGACC
88 A E D T A V Y Y C A R G D Y R Y N G D W

1201 TTCTTCGACG TCTGGGGTCA AGGAACCCTG GTCACCGTCT CCTCGGCCTC CACCAAGGGC
AAGAAGCTGC AGACCCCACT TCCCTGGGAC CAGTGGCAGA GGAGCCGGAG GTGGTTCCCG
108 F F D V W G Q G T L V T V S S A S T K G

1261 CCATCGGTCT TCCCCCTGGC ACCCTCCTCC AAGAGCACCT CTGGGGGCAC AGCGGCCCTG
GGTAGCCAGA AGGGGGACCG TGGGAGGAGG TTCTCGTGGA GACCCCGCTG TCGCCGGGAC
128 P S V F P L A P S S K S T S G G T A A L

1321 GGCTGCCTGG TCAAGGACTA CTTCCCCGAA CCGGTGACGG TGTCGTGGAA CTCAGGCGCC
CCGACGGACC AGTTCTTGAT GAAGGGGCTT GGCCACTGCC ACAGCACCTT GAGTCCGCGG
148 G C L V K D Y F P E P V T V S W N S G A

1381 CTGACCAGCG GCGTGCACAC CTTCCCGGCT GTCCTACAGT CCTCAGGACT CTA CTCCCTC
GACTGGTGC CACGCTGTG GAAGGGCCGA CAGGATGTCA GGAGTCTGA GATGAGGGAG
168 L T S G V H T F P A V L Q S S G L Y S L

1441 AGCAGCGTGG TGACCGTGCC CTCCAGCAGC TTGGGCACCC AGACCTACAT CTGCAACGTG
TCGTGCGACC ACTGGCACGG GAGGTCGTG AACCCTGGG TCTGGATGTA GACGTTGCAC
188 S S V V T V P S S S L G T Q T Y I C N V

1501 AATCACAAGC CCAGCAACAC CAAGGTGCGAC AAGAAAGTTG AGCCCAAATC TTGTGACAAA
TTAGTGTTTC GGTGCTGTG GTTCCAGCTG TTCTTTCAAC TCGGGTTTAG AACACTGTTT
208 N H K P S N T K V D K K V E P K S C D K

1561 ACTCACACAT GCCCGCCGTGA
TGAGTGTGTA CGGGCGGCACT
228 T H T C P P O

FIG. 53

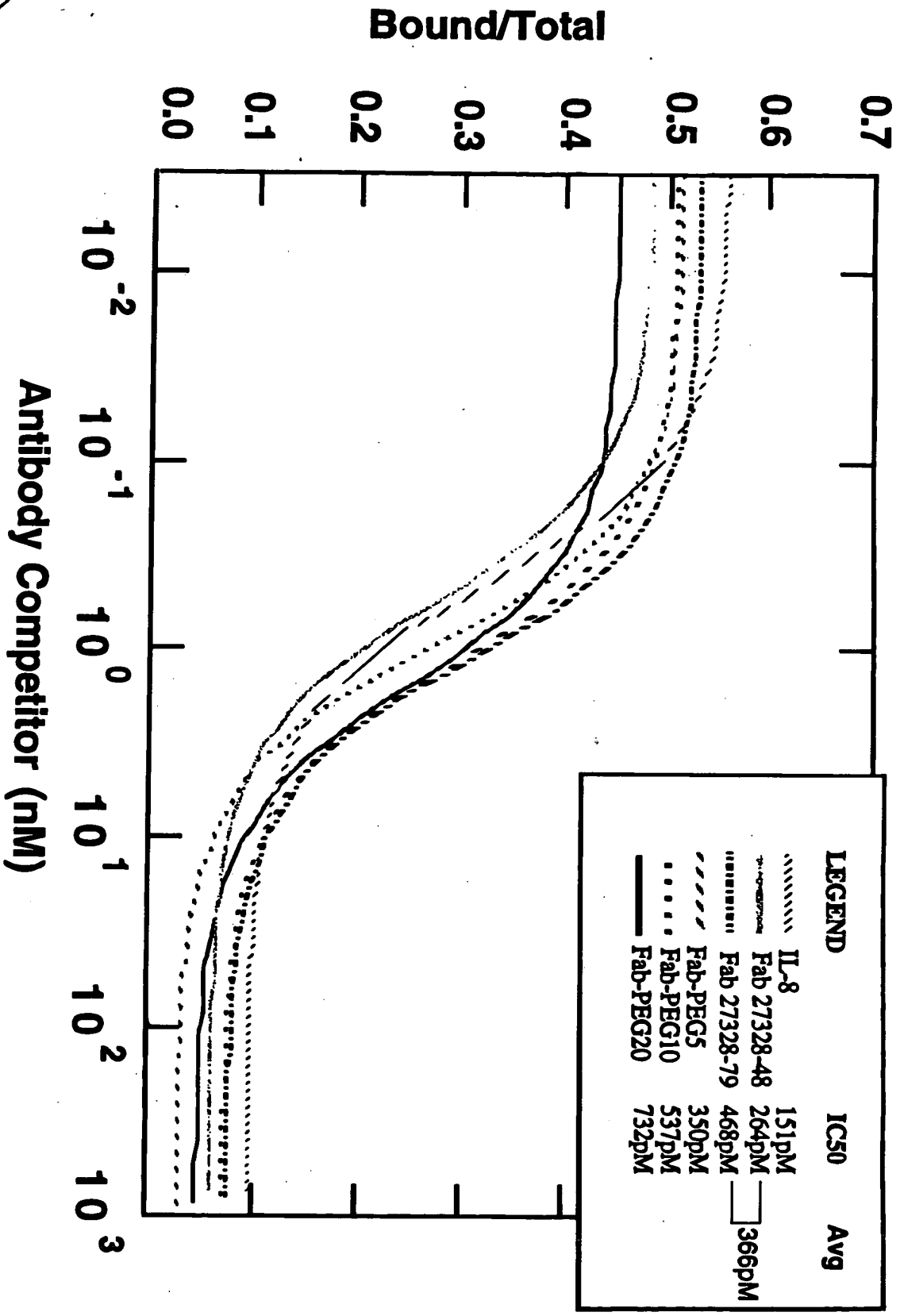
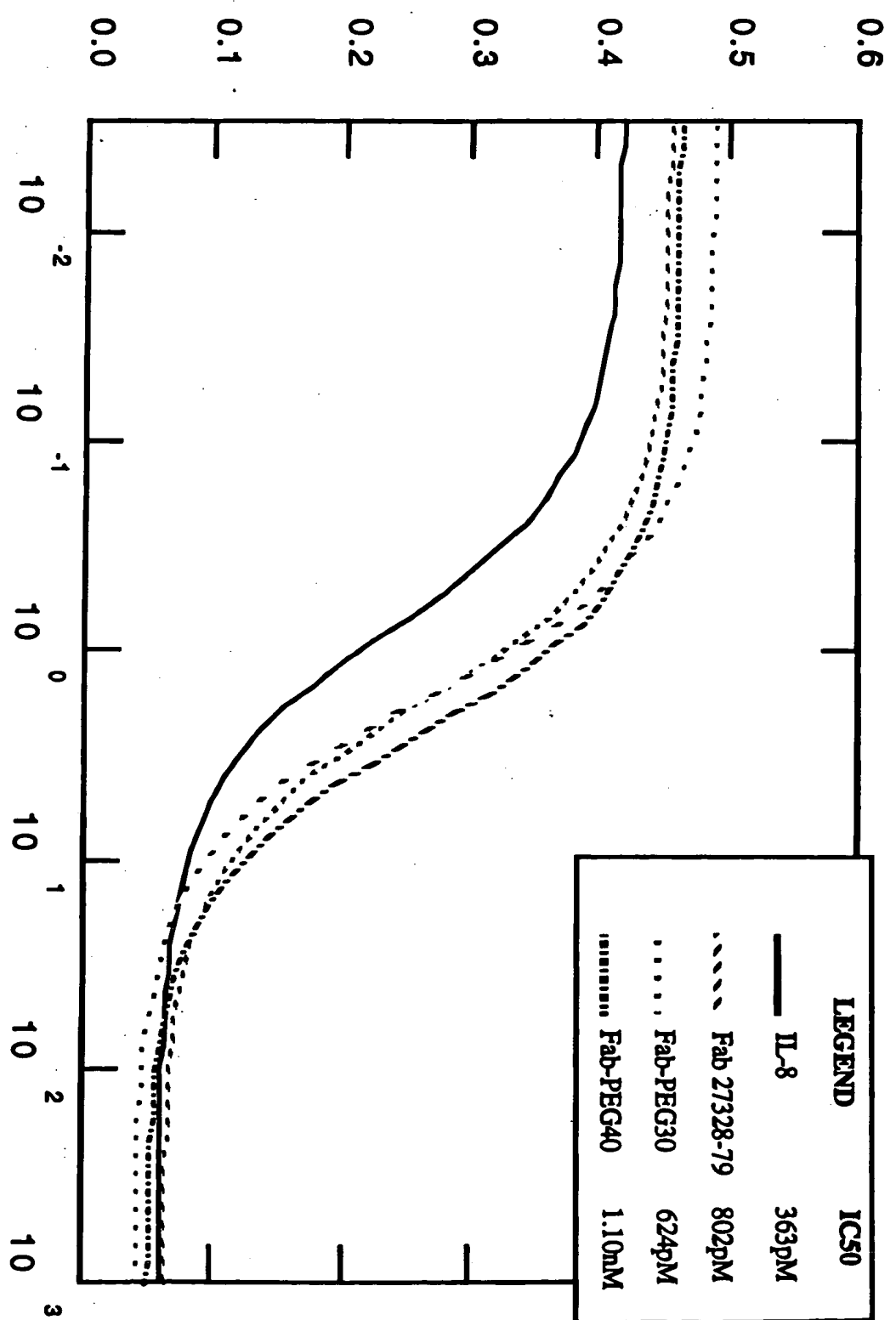


FIG. 54A



Bound/Total



Antibody Competitor (nM)

FIG. 54B

LEGEND		IC50
—	IL-8	363pM
- - -	Fab 27328-79	802pM
.....	Fab-PEG30	624pM
	Fab-PEG40	1.10nM

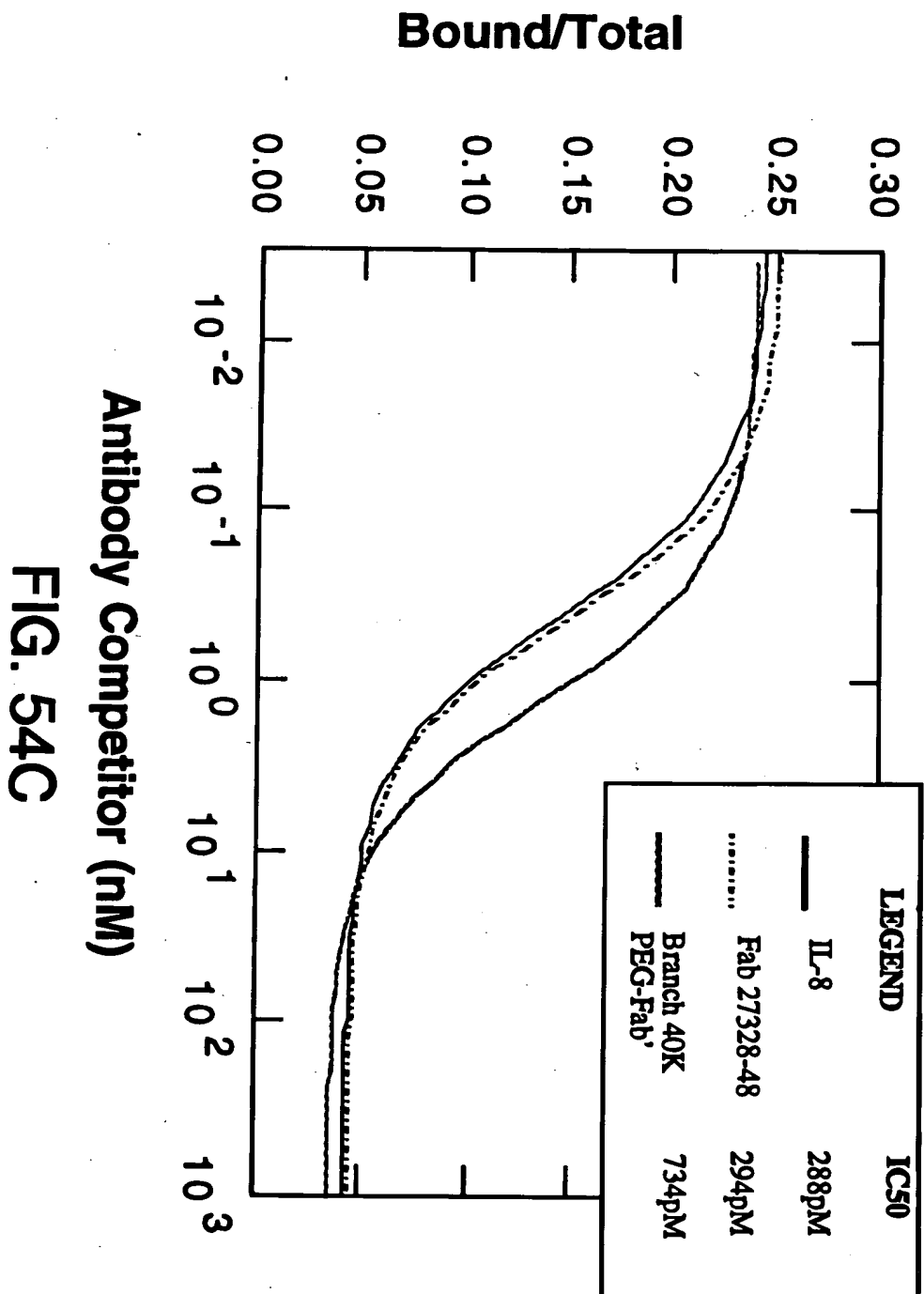


FIG. 54C

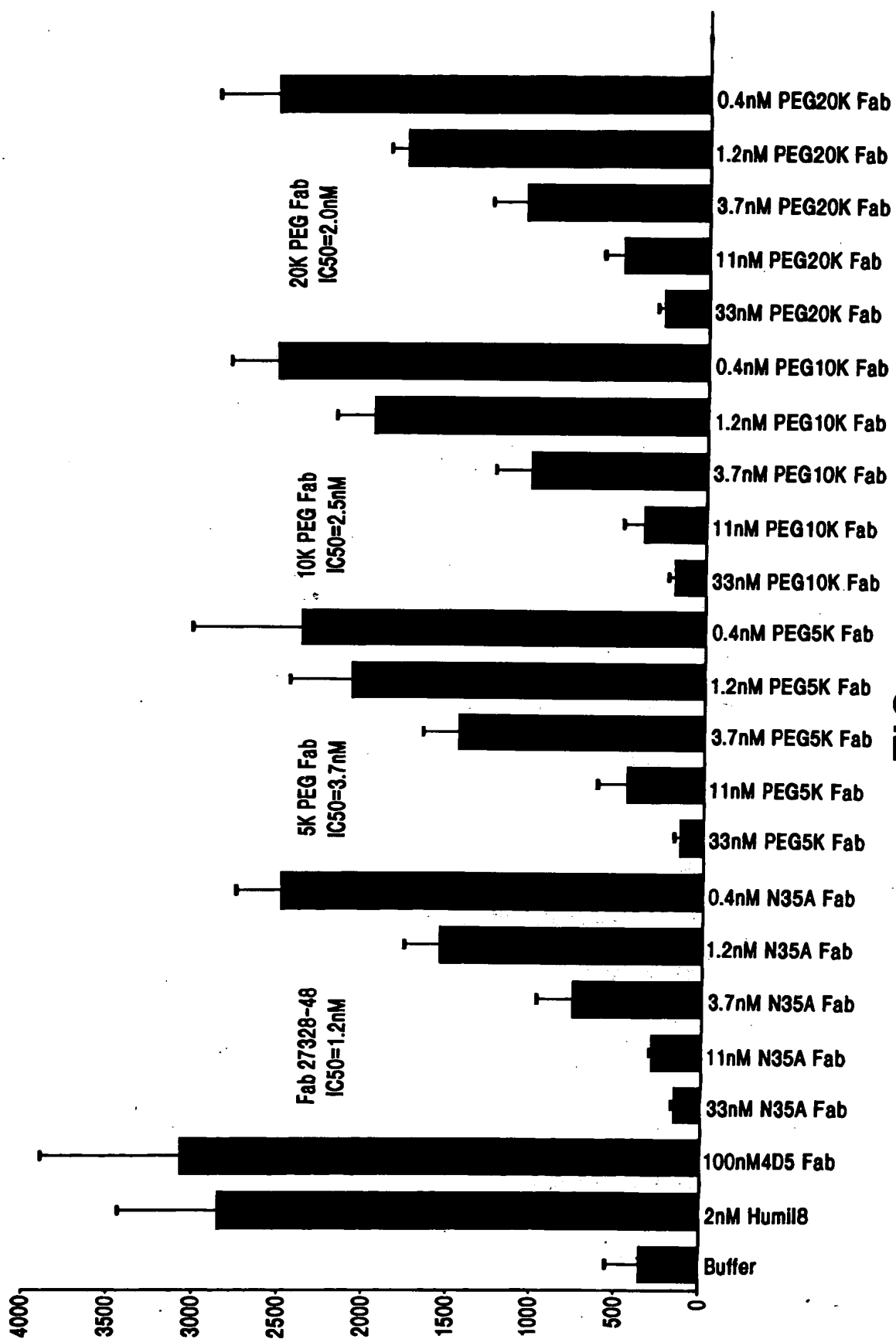


FIG. 55A

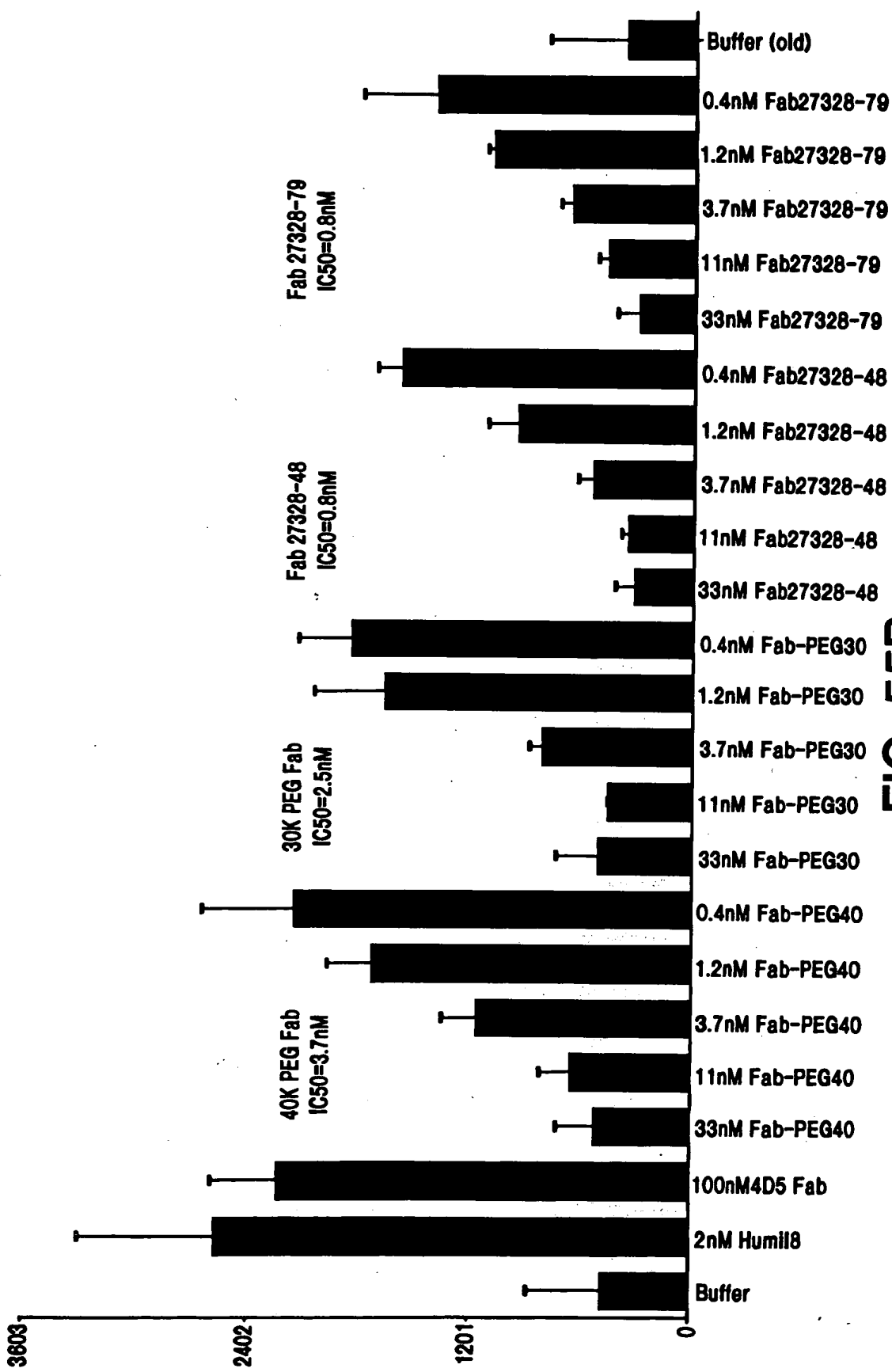


FIG. 55B

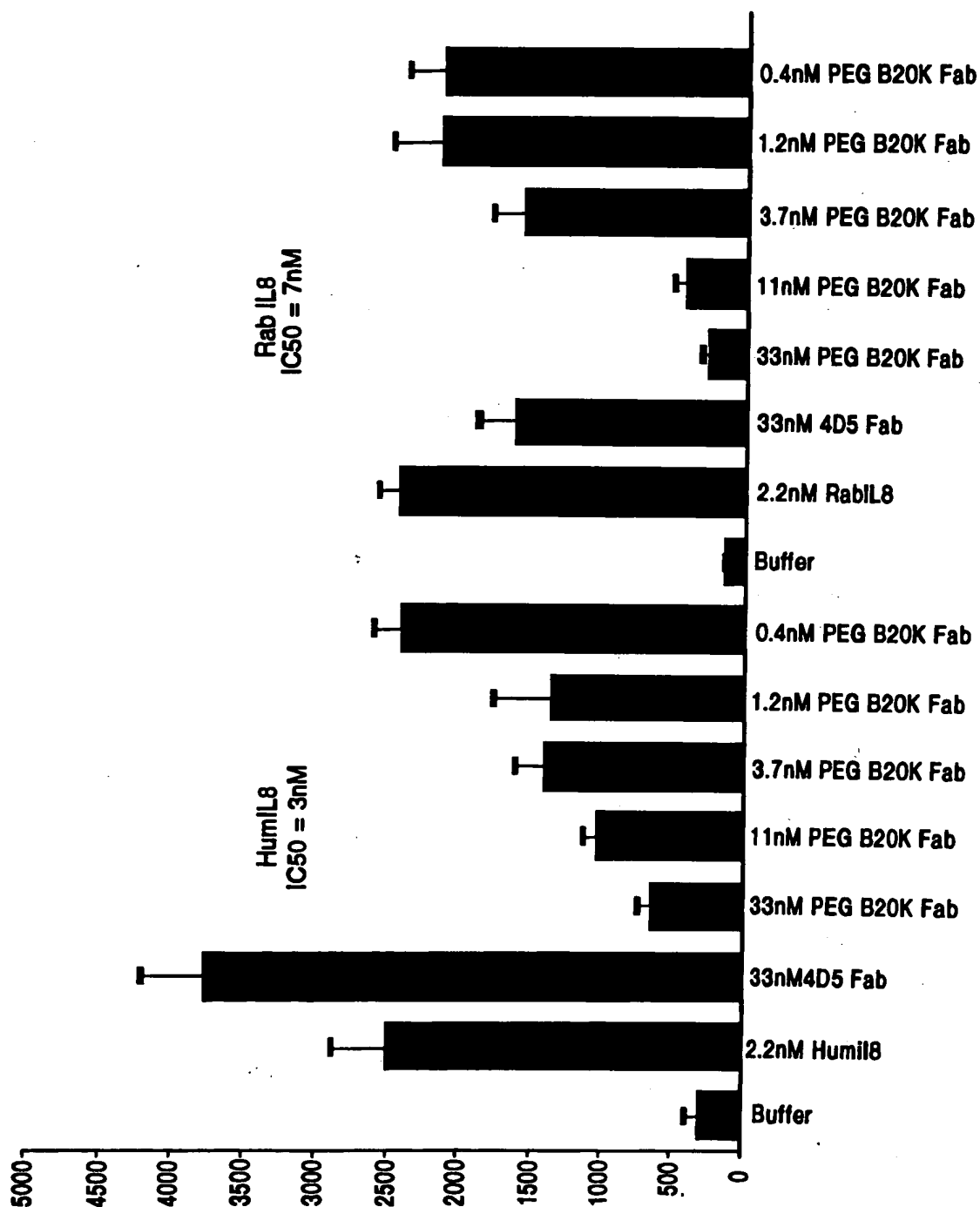


FIG. 55C



% Total Cellular β -Glucuronidase

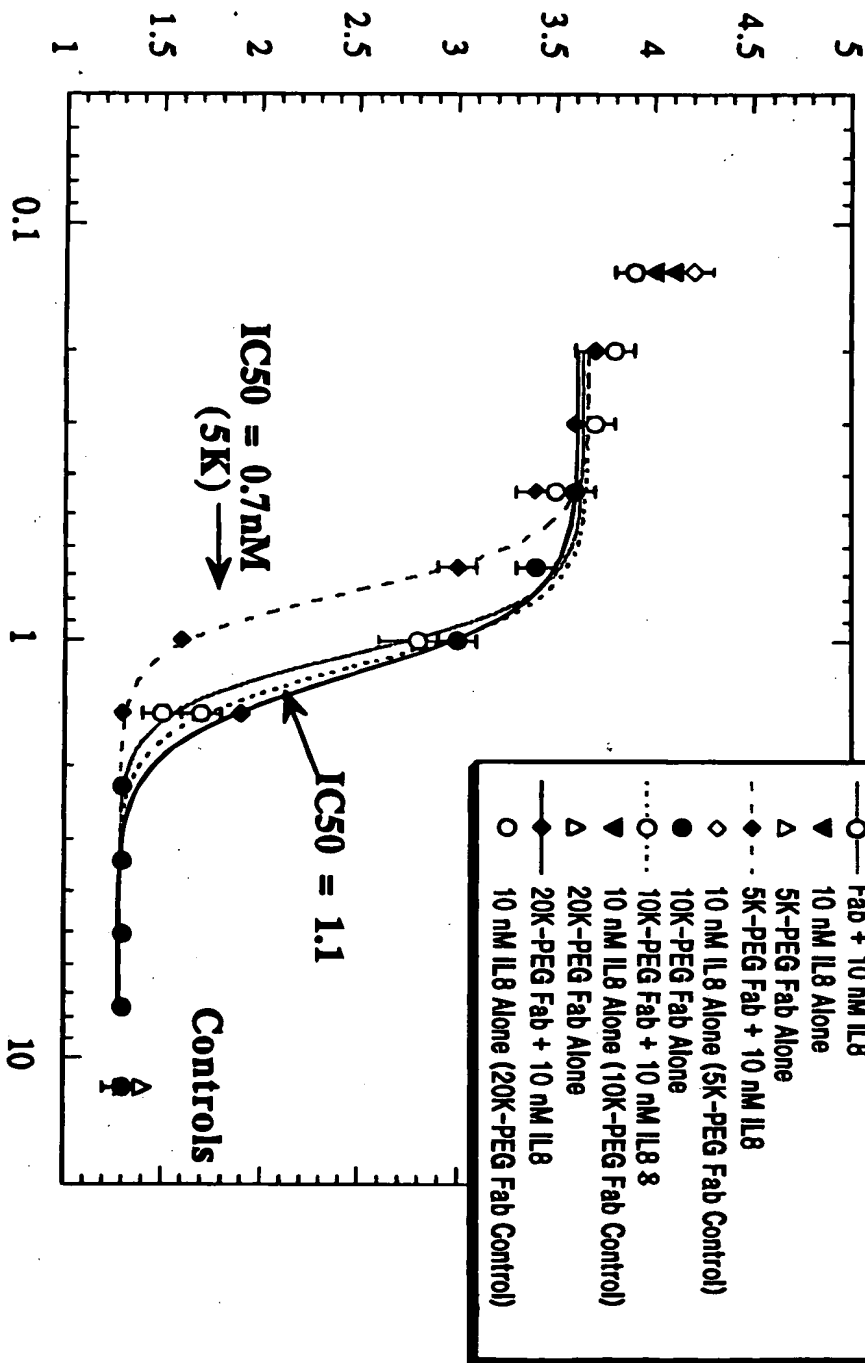
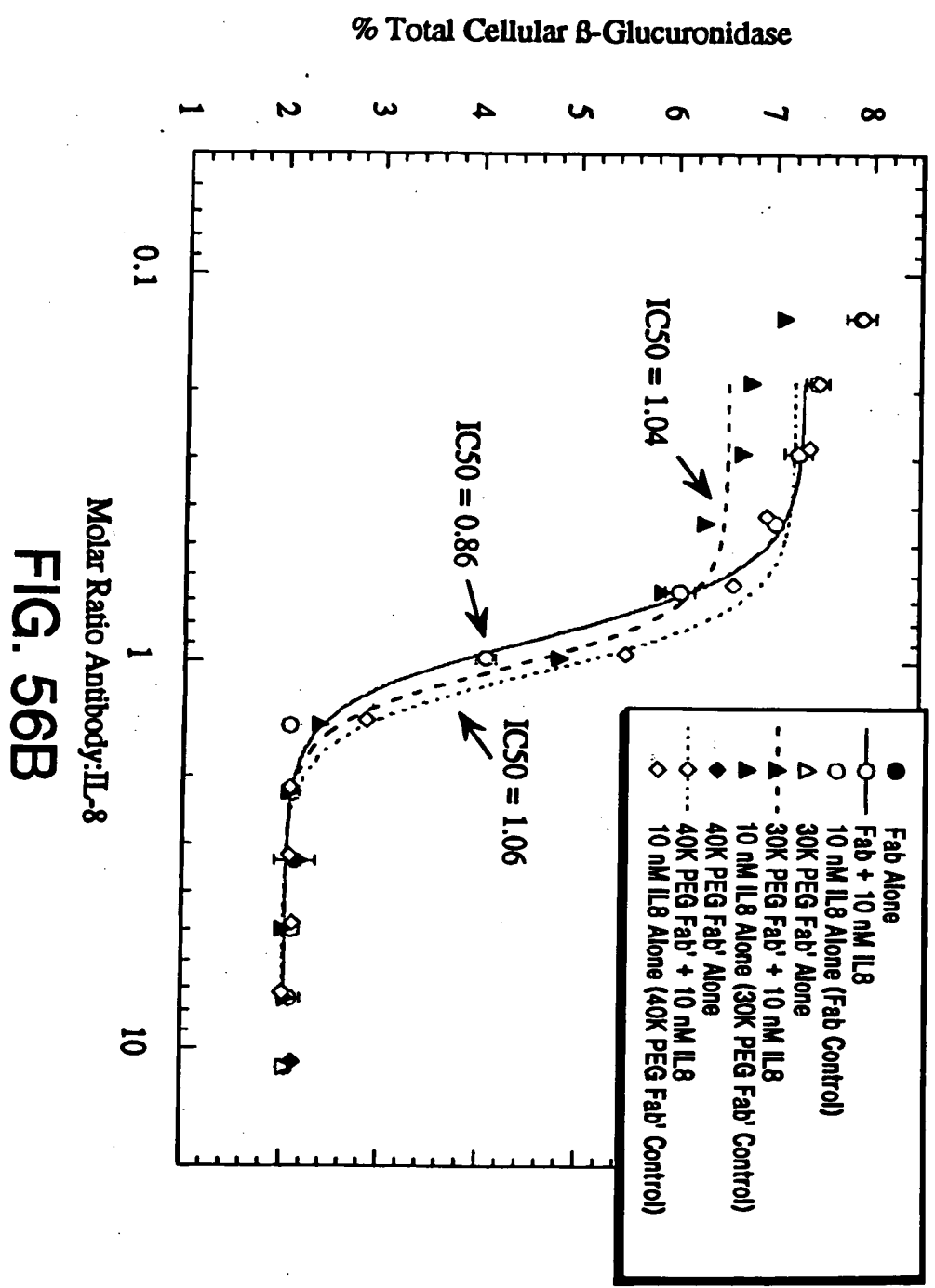


FIG. 56A



% Total Cellular β -Glucuronidase Activity

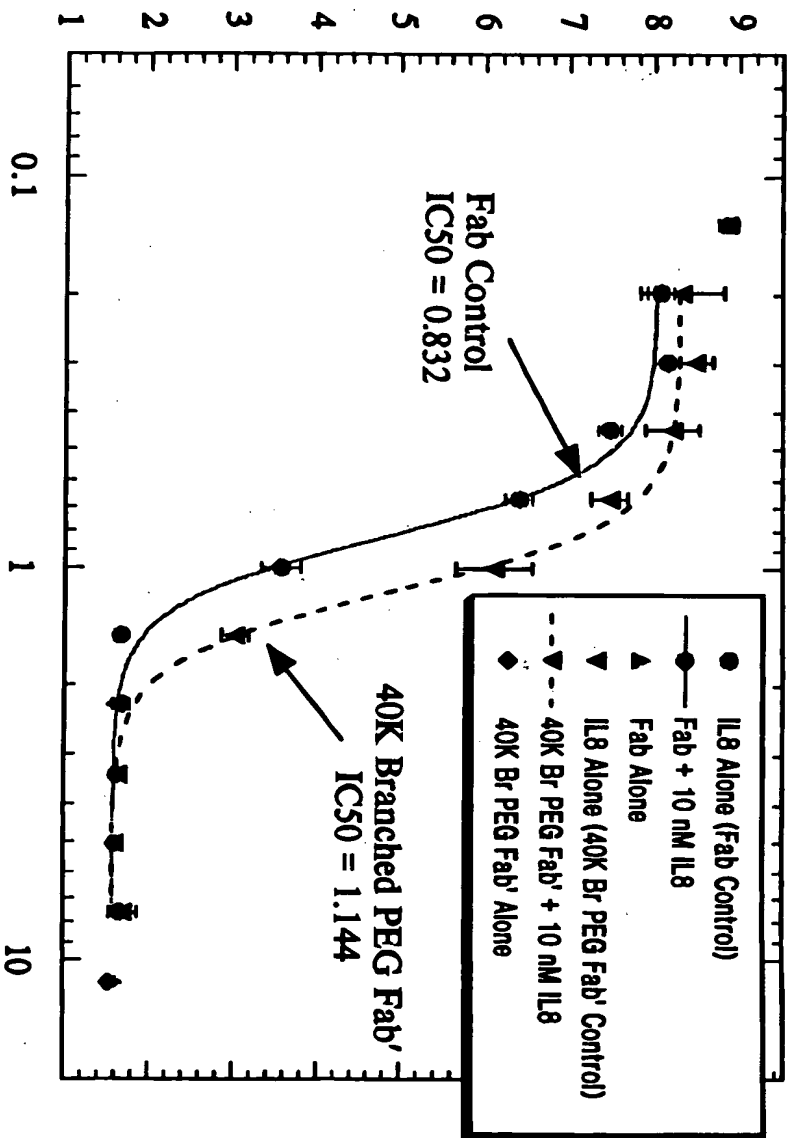
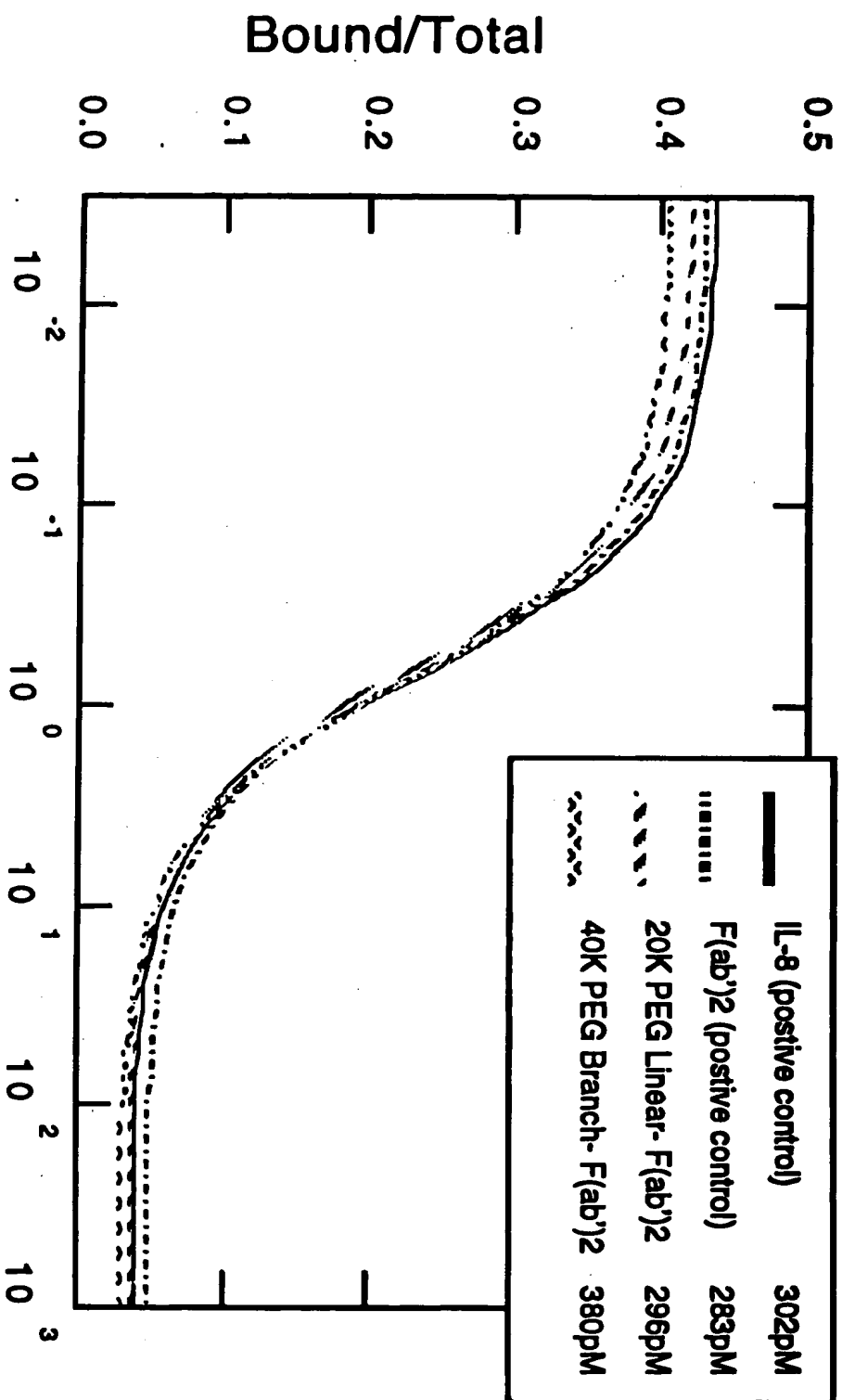
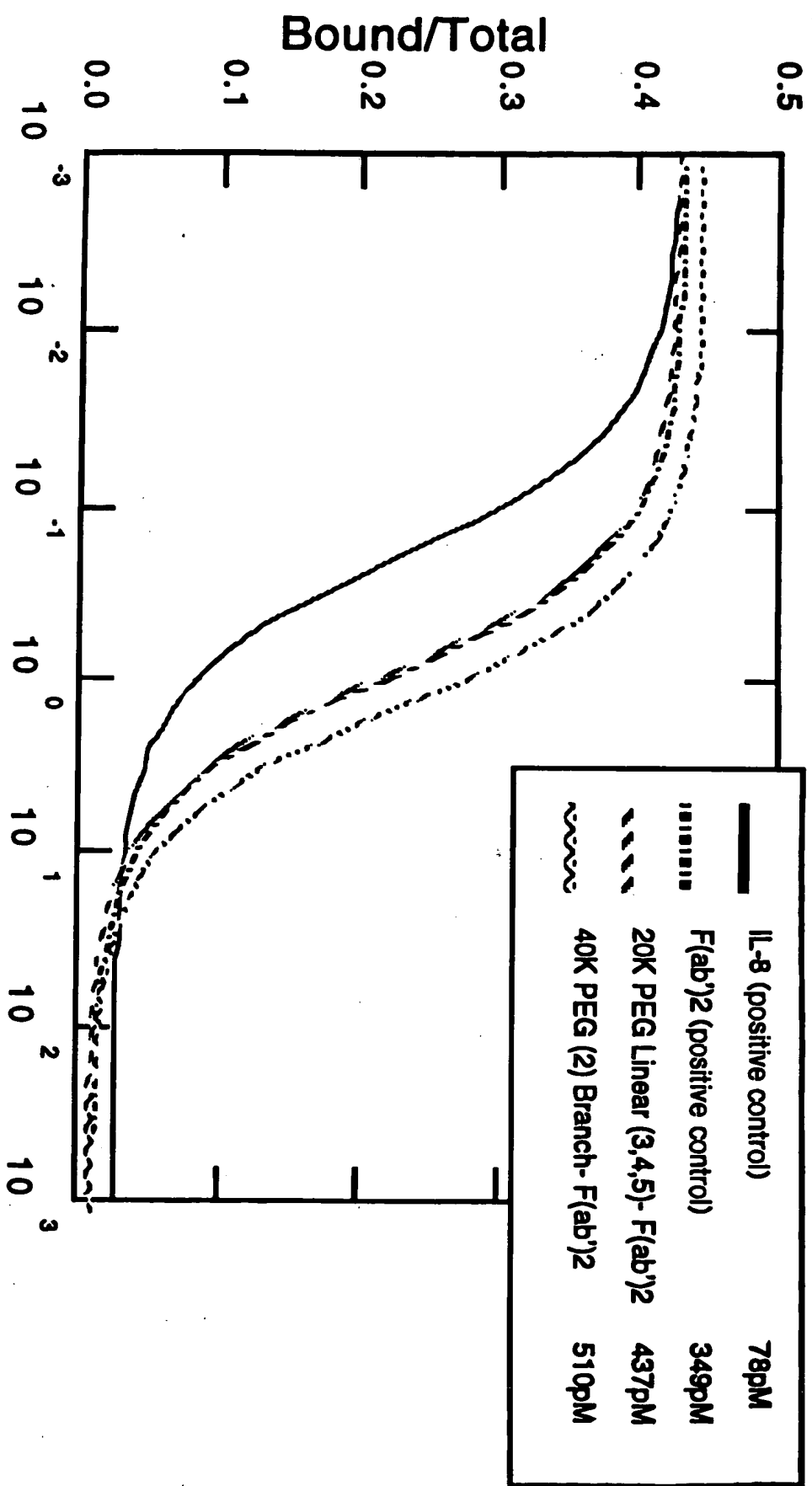


FIG. 56C



Pegylated F(ab')₂ (nM)
FIG. 57A



Pegylated F(ab')₂ (nM)

FIG. 57B

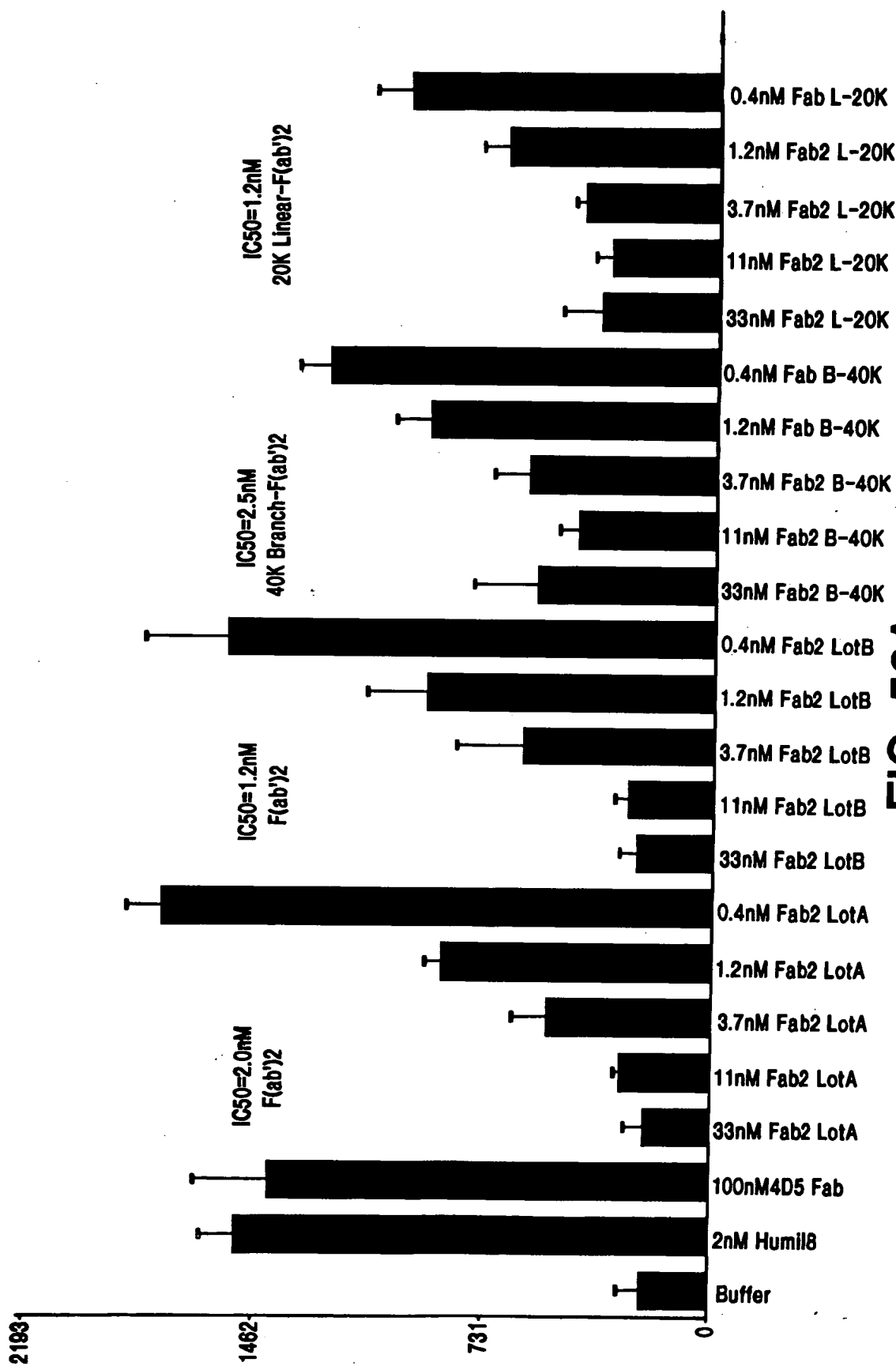


FIG. 58A

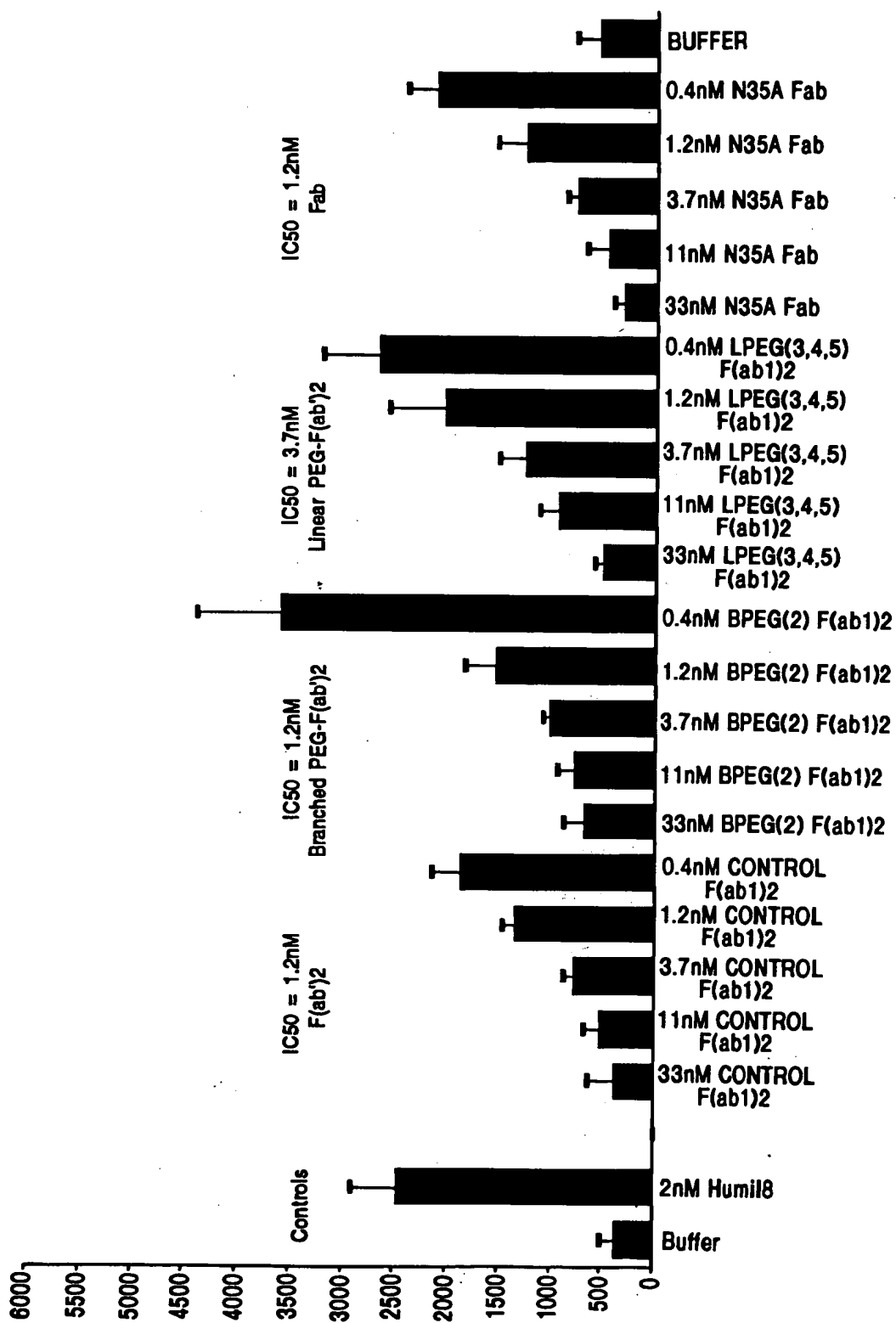
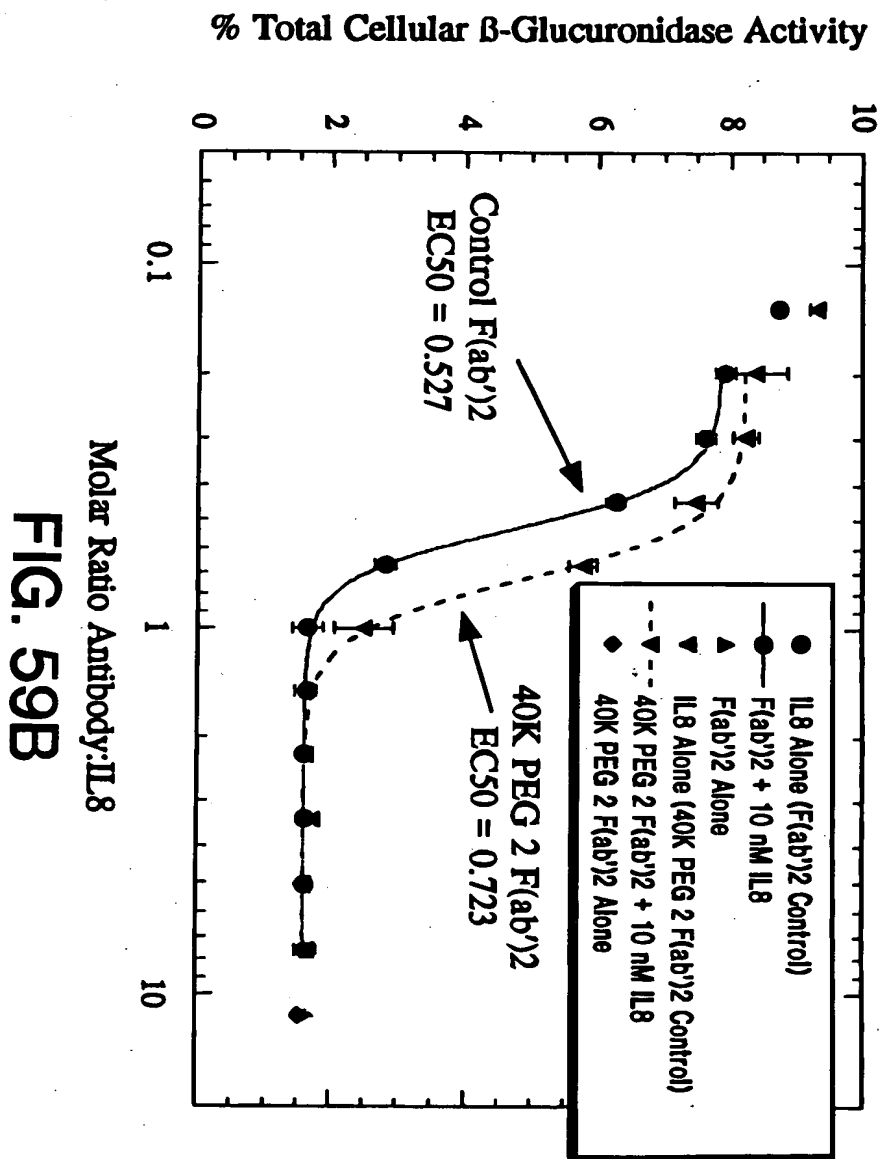
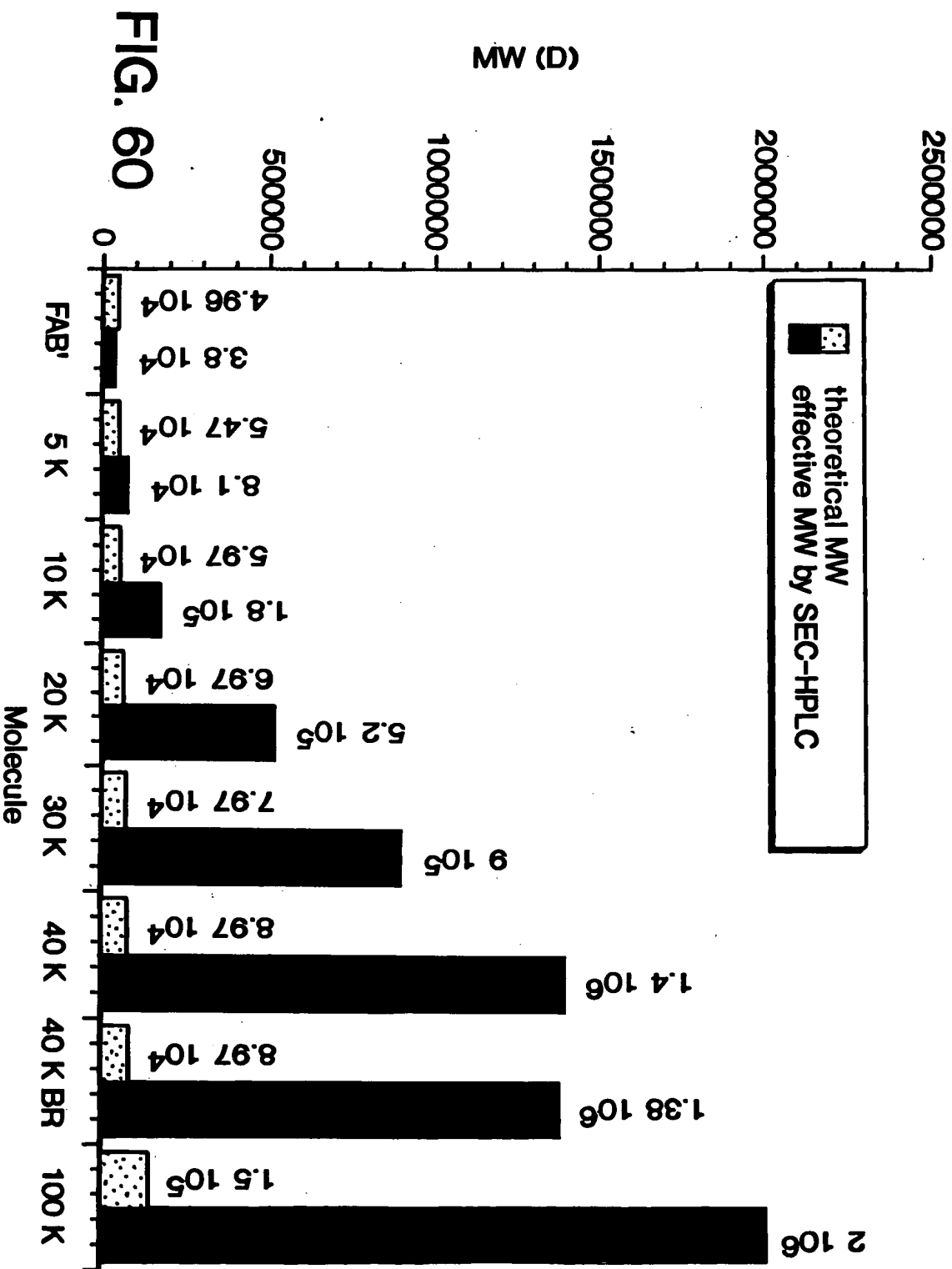
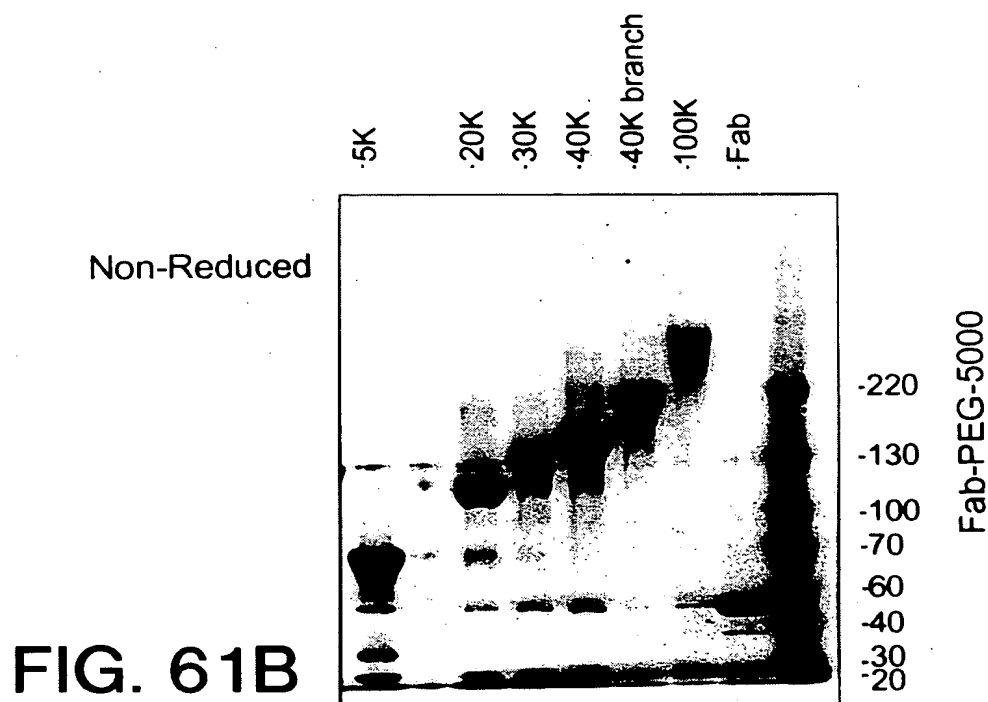
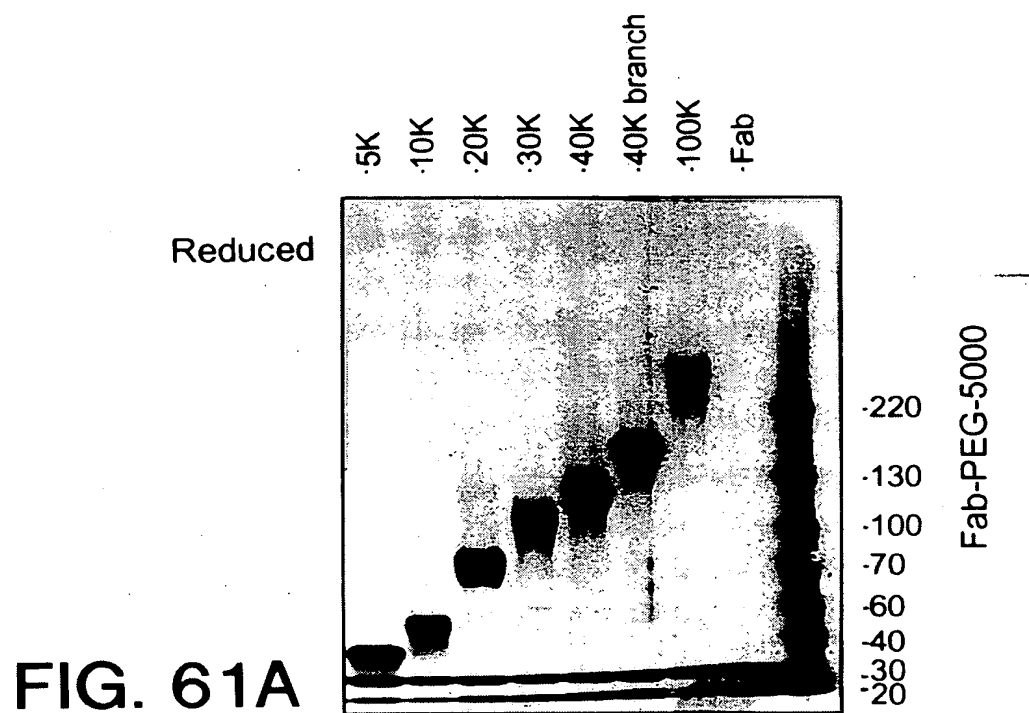


FIG. 58B







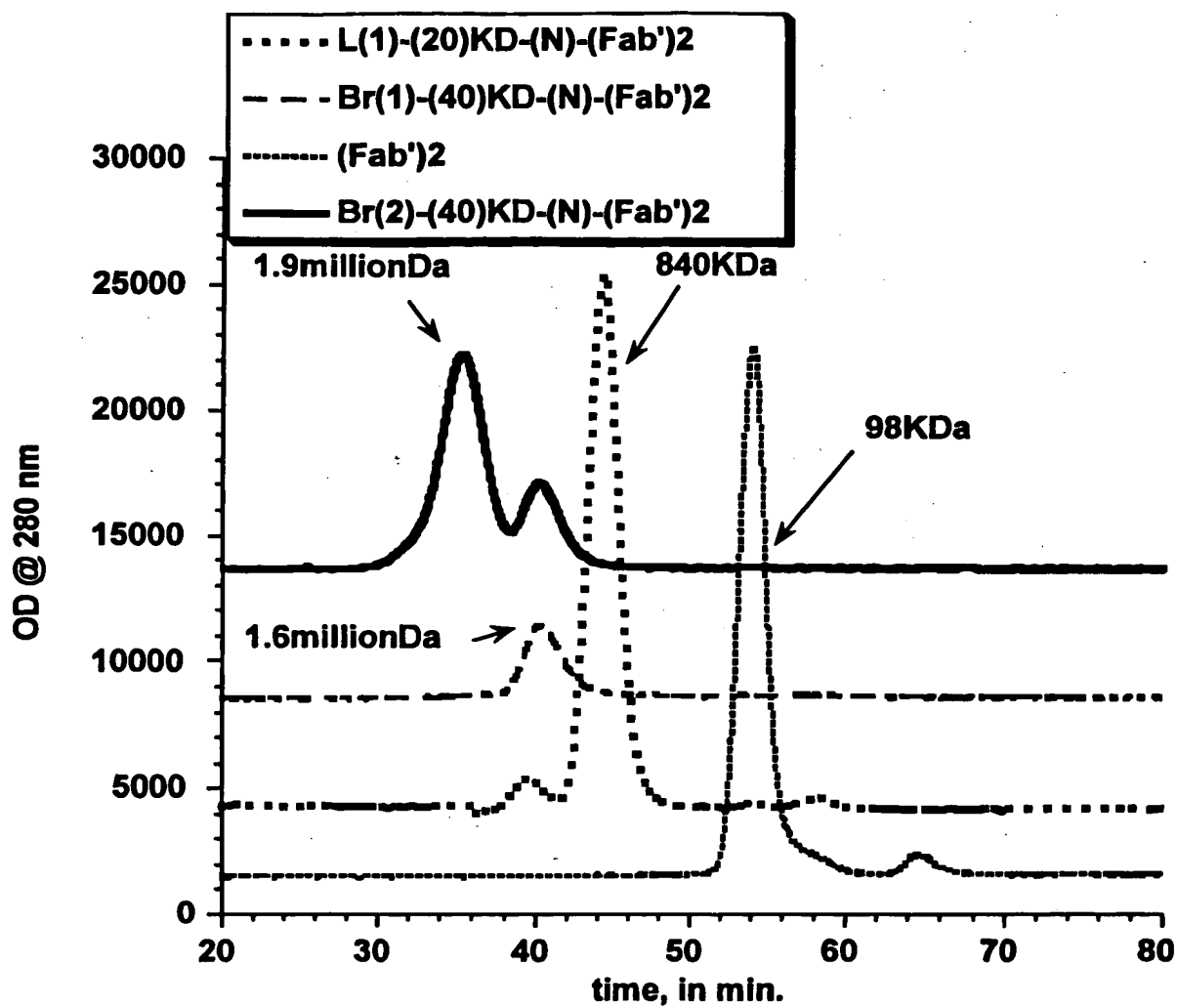


FIG. 62

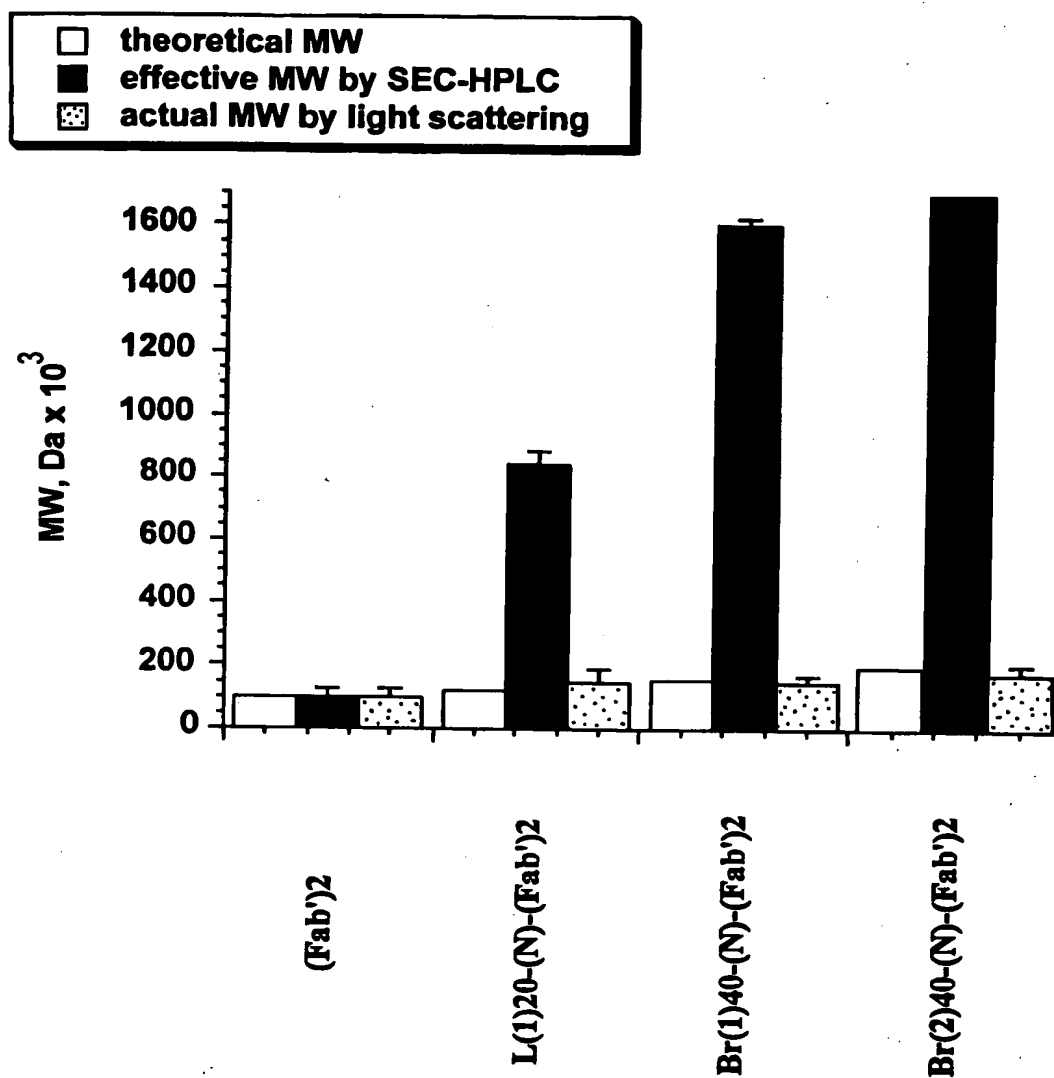


FIG. 63

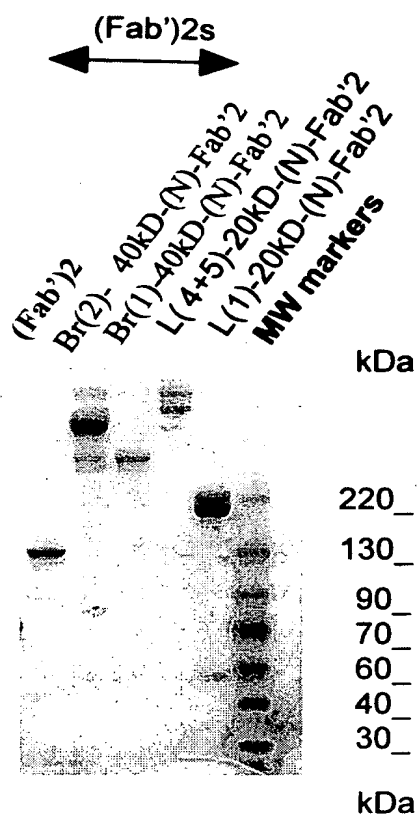
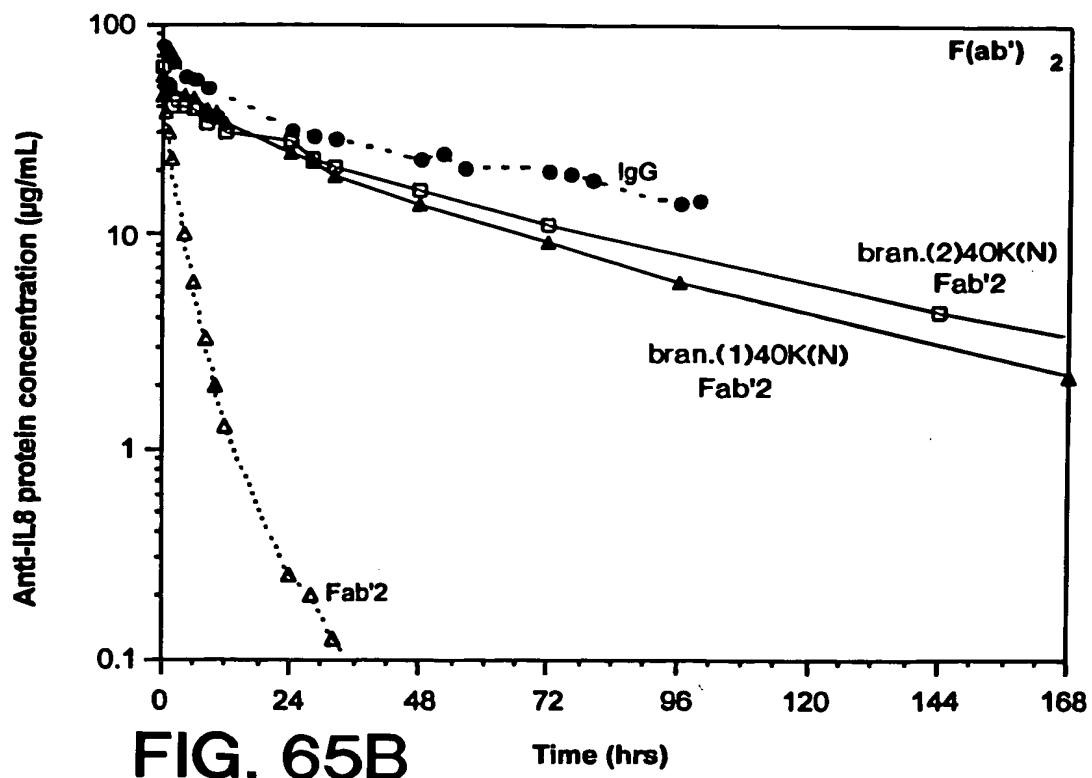
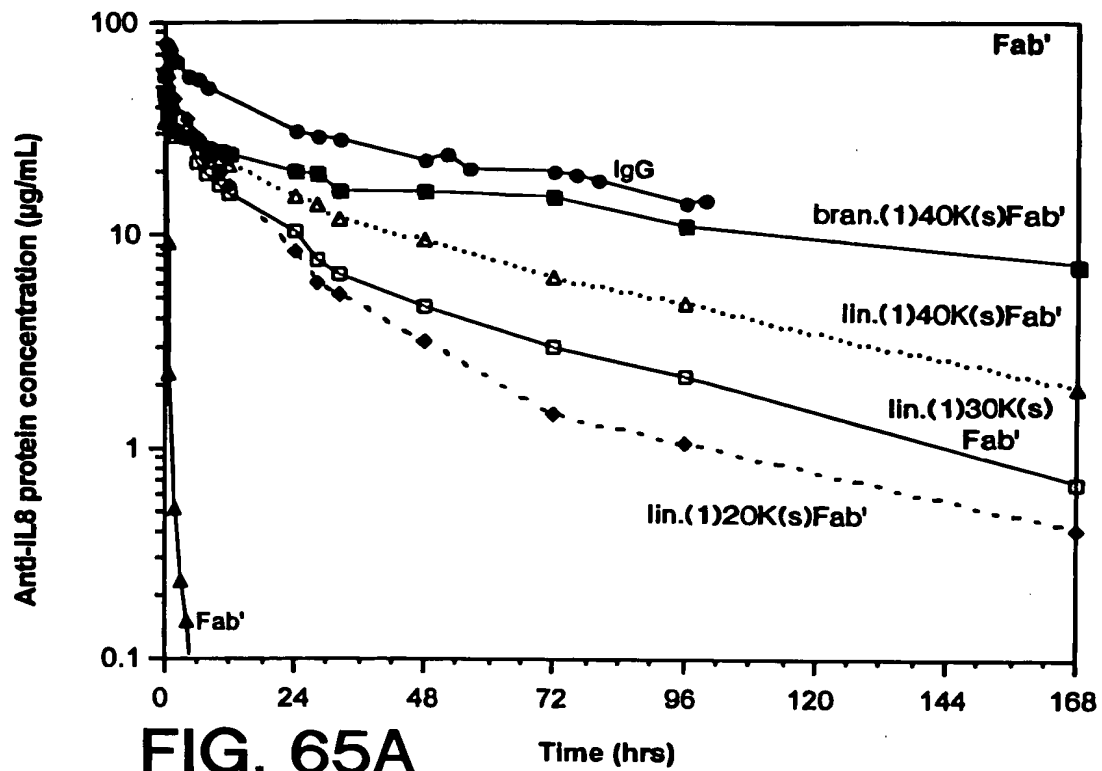


FIG. 64



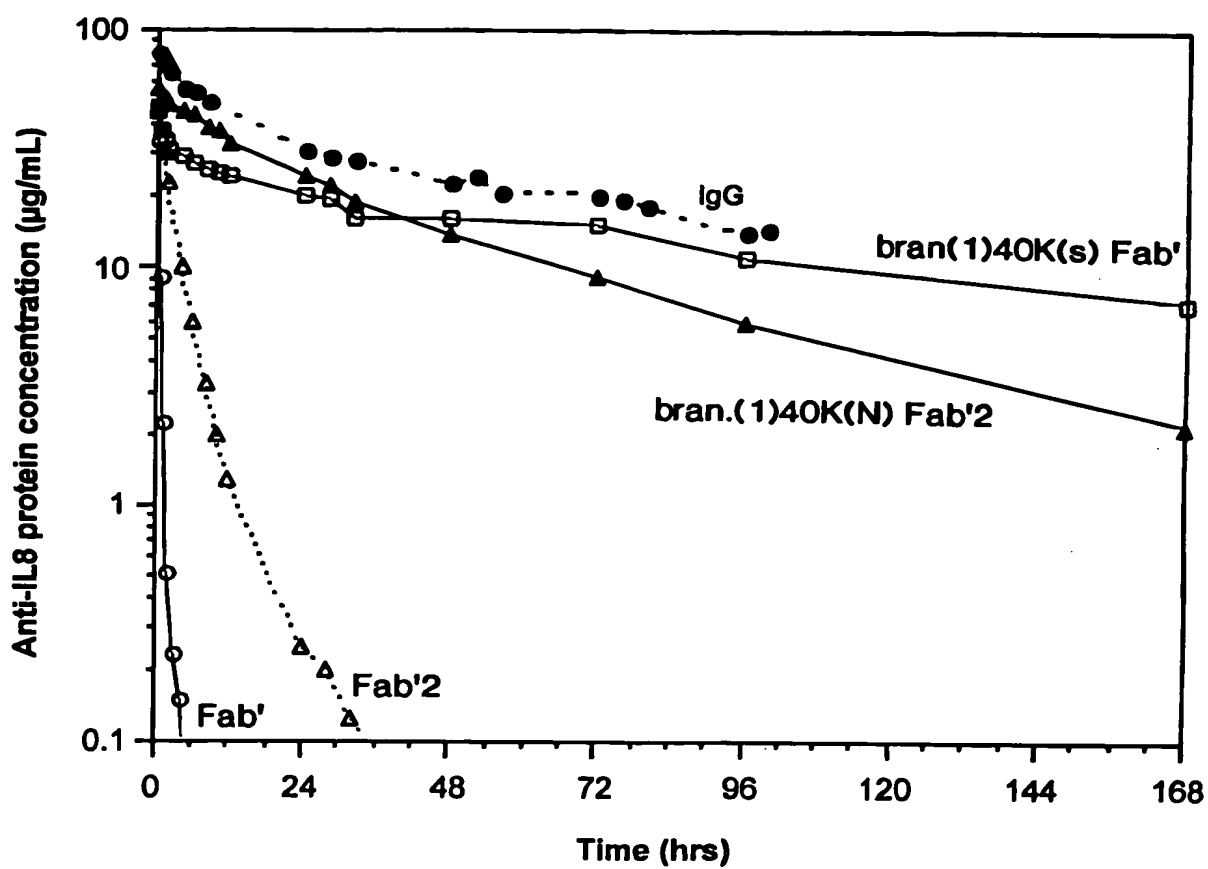


FIG. 66

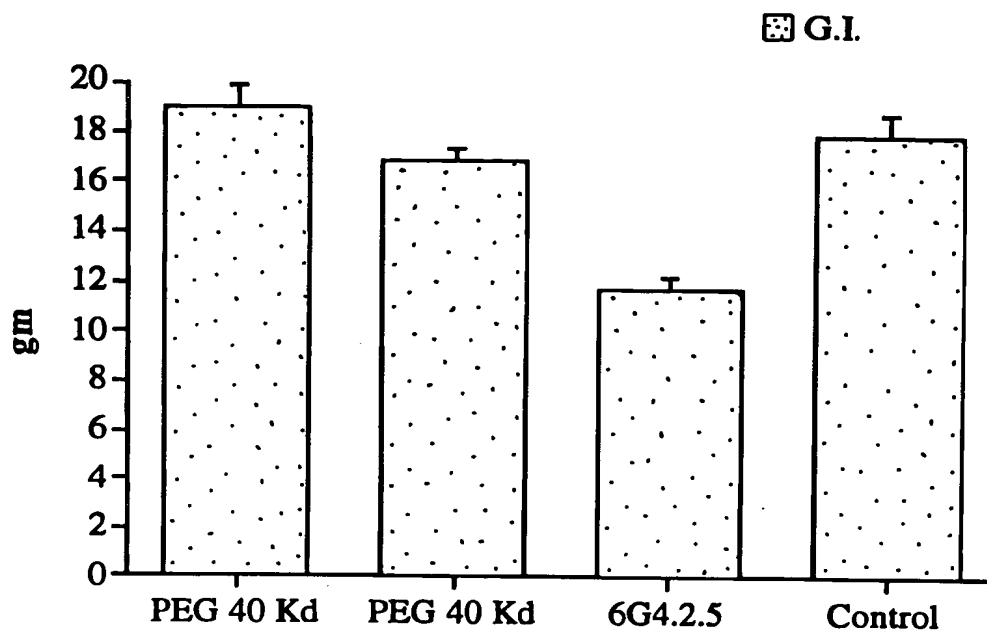


FIG. 67

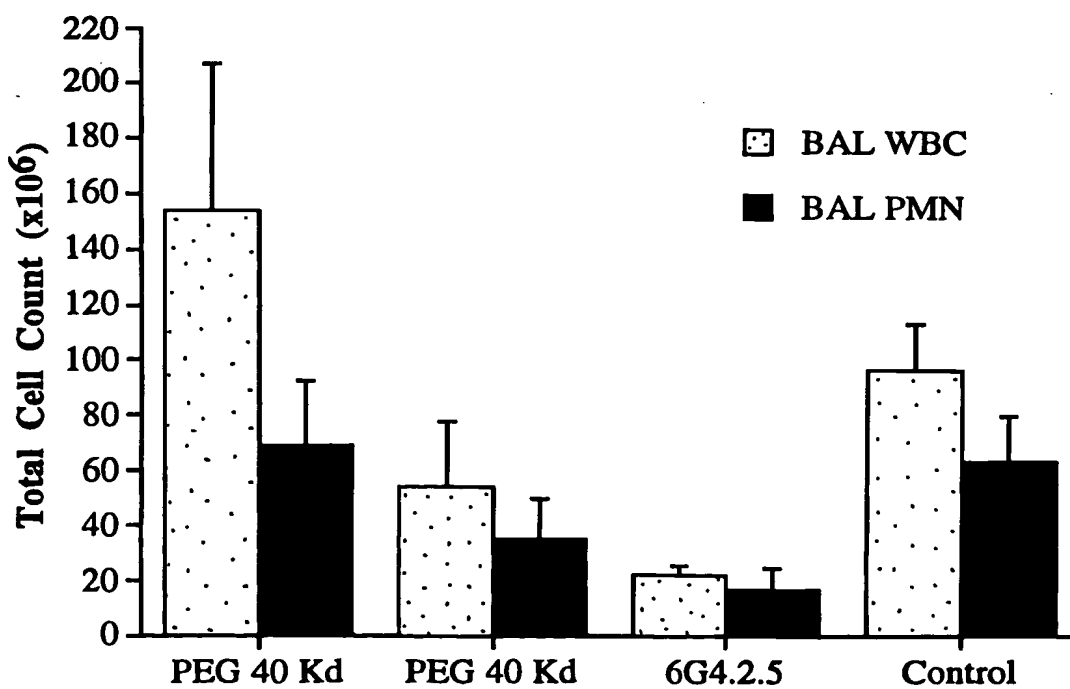


FIG. 68

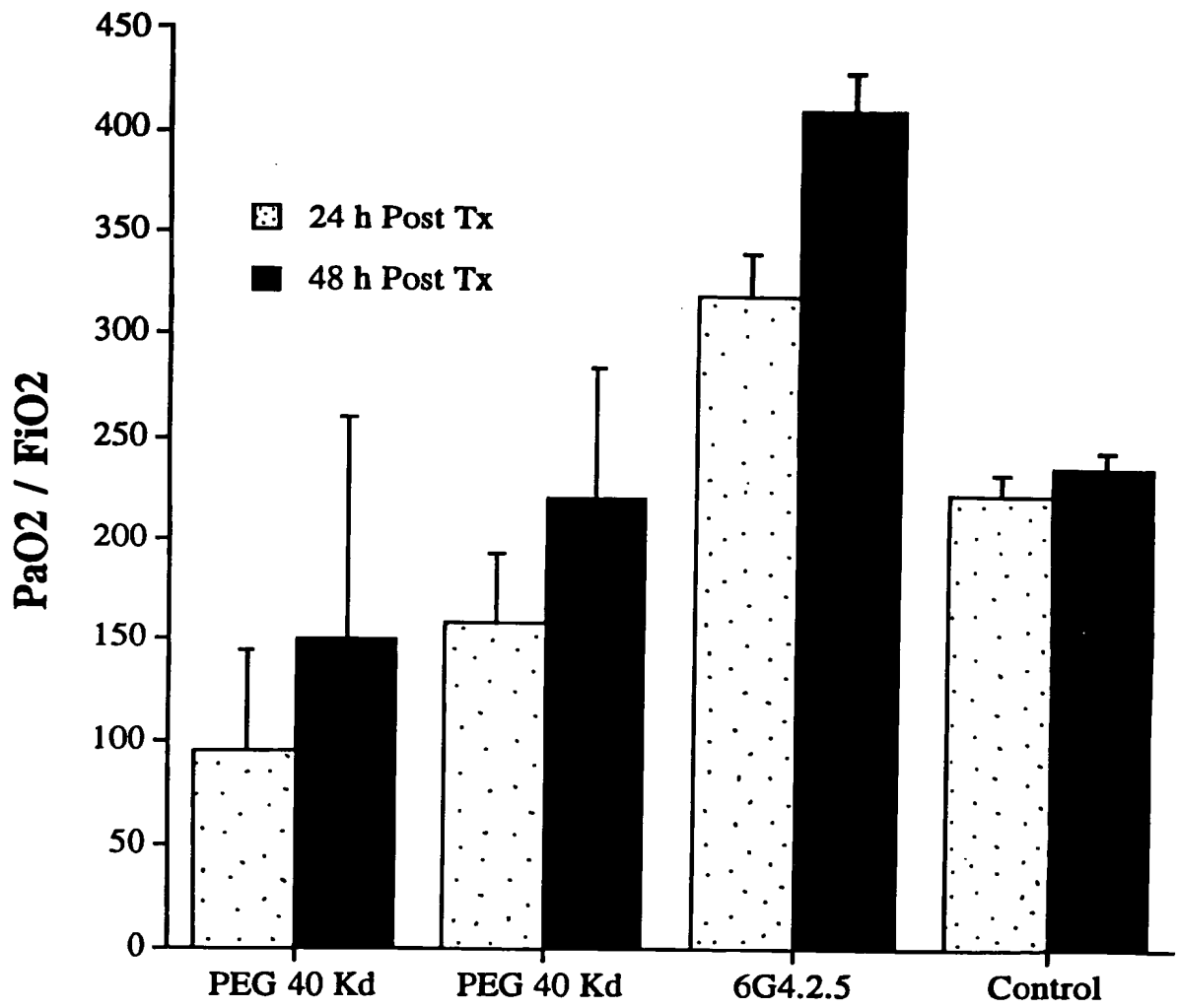


FIG. 69